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jan.delaval@uspto.gov

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=> d his

     (FILE 'HOME' ENTERED AT 08:39:27 ON 04 MAR 2003)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 08:40:07 ON 04 MAR 2003
               E METANICOTINE/CN
L1             1 S E3
               SEL RN
L2             4 S E1/CRN

     FILE 'HCAOLD' ENTERED AT 08:40:36 ON 04 MAR 2003
L3            19 S L1 OR L2

     FILE 'HCAPLUS' ENTERED AT 08:41:23 ON 04 MAR 2003
L4            48 S L1 OR L2
L5            77 S METANICOTIN?
L6            17 S PYRIDINE(S)3()4()(METHYLAMINO OR METHYL AMINO)()1()BUTENYL
L7            99 S L4-L6
               E PAPKE R/AU
L8            47 S E3,E4,E6,E7
L9             0 S L7 AND L8
               E NICOTINIC RECEPTOR/CT
               E E6+ALL
L10         7372 S E77,E78,E76+NT
L11         9279 S E81-E87/BI
L12          534 S NICOTINIC (S) RECEPTOR(S) SUBTYP?
L13         6280 S NICOTINIC (S) RECEPTOR(S) (ACETYLCHOLIN? OR ACETYL CHOLIN? OR
L14           18 S L7 AND L10-L13

     FILE 'REGISTRY' ENTERED AT 08:46:31 ON 04 MAR 2003
L15           73 S C10H14N2/MF AND NC5/ES AND 1/NR
L16           13 S L15 AND 3 BUTEN?
L17            5 S L16 AND N METHYL
L18            3 S L17 NOT (D/ELS OR 11C)
L19            2 S L18 NOT L1
               SEL RN
L20            7 S E1-E2/CRN
L21            5 S L20 NOT COMPD
L22            2 S L20 NOT L21

     FILE 'HCAPLUS' ENTERED AT 08:48:13 ON 04 MAR 2003
L23           20 S L19
L24           22 S L21
L25            3 S L22
L26           37 S L23,L24,L25
L27          117 S L7,L26
L28           30 S L10-L13 AND L27
L29        65856 S ACETYLCHOLINE
L30        23900 S NICOTINE
L31           17 S 3 2 4 DIMETHOXYBENZYLIDENE ANABASEINE
L32            4 S DMXB A
L33            7 S 2 METHYL 3 2 (1W) PYRROLIDINYLMETHOXY PYRIDINE
L34            0 S 2 METHYL 3 2 (1W) PYRROLIDINYL METHOXY PYRIDINE
L35           20 S ABT089 OR ABT 089
L36            0 S 3 METHYL S 1 METHYL 2 PYRROLIDINYL ISOXAZOLE
L37           24 S 3 METHYL (1W) 1 METHYL 2 PYRROLIDINYL ISOXAZOLE
L38           80 S ABT418 OR ABT 418
L39            7 S 5 2 AZETIDINYLMETHOXY 2 CHLOROPYRIDINE
L40            0 S 5 2 AZETIDINYL METHOXY 2 CHLOROPYRIDINE
L41           42 S ABT594 OR ABT 594
L42            5 S ALTINICLIN#
L43            0 S 4 2 1 METHYL 2 PYRROLIDINYLETHYL THIO PHENOL HYDROCHLORIDE
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L44           0 S 4 2 1 METHYL 2 PYRROLIDINYLETHYL THIOPHENOL HYDROCHLORIDE
L45           0 S 4 2 1 METHYL 2 PYRROLIDINYLETHYLTHIOPHENOL HYDROCHLORIDE
L46           3 S PYRROLIDINYLETHYLTHIOPHENOL OR PYRROLIDINYLETHYLTHIO PHENOL O
L47           9 S SIB1553A OR SIB 1553A
L48           1 S EPIBATADIN#
L49         576 S EPIBATIDIN#
L50        1953 S MECAMYLAMINE

     FILE 'REGISTRY' ENTERED AT 08:58:39 ON 04 MAR 2003
L51           1 S 51-84-3
L52           1 S 54-11-5
L53          67 S C10H14N2/MF AND NC4/ES AND NC5/ES AND 1/NC AND 2 PYRROLIDINYL
L54          10 S L53 NOT (LABELED OR ION OR 11C# OR 13C# OR 14C# OR C11# OR C1
L55           4 S L54 AND 3
L56          20 S L53 AND NICOTINE
L57           5 S L56 AND L54
                 SEL RN 2 4
L58           3 S L57 NOT E3-E4
L59           4 S L51,L52,L58
L60           1 S L55 NOT L59
L61           5 S L59,L60
L62           1 S 156223-05-1
L63           3 S C19H20N2O2/MF AND 46.150.18/RID AND NC5/ES AND 3/NR AND 2 4 D
L64           1 S 148372-04-7
L65           1 S 148372-04-7/CRN
L66           1 S 161417-03-4
L67          71 S C11H16N2O/MF AND NC4/ES AND NC5/ES
L68           2 S L67 AND 2 PYRROLIDINYLMETHOXY AND 2 METHYL 3
L69           1 S 147402-53-7
L70          10 S C9H14N2O/MF AND NC4/ES AND NOC3/ES
L71           7 S L70 AND 3 METHYL 5
L72           3 S L71 AND 1 METHYL 2
L73           1 S 179120-92-4
L74           4 S C12H14N2/MF AND NC4/ES AND NC5/ES AND 3 ETHYNYL 5
L75           3 S L74 AND 1 METHYL 2
L76           1 S 191611-89-9
L77           1 S 191611-76-4
L78           2 S 140111-52-0 OR 152378-30-8
L79          15 S C11H13CLN2/MF AND 46.156.30/RID AND 103.39.1/RID
L80          10 S L79  AND 6 CHLORO 3
L81           9 S L80 AND 2 6 CHLORO
L82           1 S 826-39-1
L83           1 S 60-40-2
L84           1 S 198283-73-7
L85           9 S C9H11CLN2O/MF AND NC5/ES AND NC3/ES
L86           5 S L85 AND 2 CHLORO
L87           3 S L86 AND 5
L88           2 S L87 NOT 1 METHYL
L89          30 S L61,L62,L64,L65,L66,L68,L69,L72,L73,L75,L76,L77,L78,L81,L82,L
                 SEL RN
L90         402 S E4-E34/CRN
L91         121 S L90 NOT (MXS/CI OR COMPD OR WITH)
L92          84 S L91 NOT (IUM OR CONJUGATE OR COMPLEX)
L93          83 S L92 NOT FE/ELS
L94          79 S L93 NOT CD/ELS
L95          37 S L91 NOT L92
L96          30 S C7H16NO2 AND L95

     FILE 'HCAPLUS' ENTERED AT 10:01:53 ON 04 MAR 2003
L97       43193 S L89 OR L94
L98        2202 S L95,L96
L99          54 S L27 AND L97,L98
L100         16 S L27 AND L31-L50
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L101          87 S L27 AND L29,L30
L102          96 S L28,L99-L101
                 E NERVOUS SYSTEM/CT
L103       18878 S NERVOUS SYSTEM/CT (L) (DISORDER OR DISEASE OR DYSFUNCTION)
L104       80095 S ?ALZHEIMER? OR ?PARKINSON? OR ?HUNGTINGTON? OR ?CHOREA? OR ?D
L105       33352 S ?ANXIET? OR ?ANXIOLYT? OR ADDICT? OR (SUBSTANCE OR DRUG OR AL
L106          16 S L27 AND L103-L105
                 E MENTAL/CT
                 E E4+ALL
L107       27751 S E2+NT
L108      144833 S E10+NT OR E11+NT OR E12+NT
                 E E12+ALL
L109        2484 S E5
                 E E51
L110       26798 S E23-E77
L111        5763 S E3-E22
L112          11 S L27 AND L107-L111
L113          20 S L106,L112
L114          17 S L102 AND L113
L115          24 S RJR2403 OR RJR 2403
L116          18 S L115 AND L27
L117         123 S L27,L115,L116
L118         101 S L117 AND L10-L13,L29-L50,L97,L98
L119          18 S L118 AND L103-L105,L108-L111
L120           2 S L119 NOT L114
L121         105 S L118-L120,L102,L112-L116
L122          32 S L121 AND (COMPOSITION OR COMBIN? OR MIX? OR SYNERG? OR FORMUL
L123          26 S L122 AND L4,L26
L124          16 S L123 AND L97,L98
L125          10 S L123 NOT L124
L126          73 S L121 NOT L122
L127          18 S L118-L121 AND P/DT
L128          24 S L27 AND P/DT
L129          24 S L127,L128 AND L4-L14,L23-L50,L97-L128
                 SEL DN AN 21-24
L130          20 S L129 NOT E1-E12

     FILE 'EMBASE' ENTERED AT 10:47:44 ON 04 MAR 2003
L131          50 S L117
L132          24 S L131 AND (F1. OR F2. OR F3. OR F4.)/CT
                 E NERVOUS SYSTEM/CT
L133          35 S L131 AND (E3+NT OR E7+NT OR E11+NT OR E12+NT)
L134           1 S L131 AND (E13+NT OR E22+NT OR E35+NT)
L135           2 S L131 AND E75+NT
                 E NERVE/CT
L136           2 S L131 AND E3+NT
L137           6 S L131 AND E50+NT
L138           0 S L131 AND E55+NT
L139           1 S L131 AND E87+NT
L140           0 S L131 AND (E101+NT OR E105+NT)
L141           0 S L131 AND (E108+NT OR E114+NT OR E120+NT)
L142           0 S L131 AND (E132 OR E137+NT)
L143           2 S L131 AND (E146+NT OR E150+NT OR E154+NT)
L144           0 S L131 AND (E164+NT OR E169+NT OR E178)
L145           0 S L131 AND E186+NT
L146           0 S L131 AND E235+NT
L147           0 S L131 AND E263+NT
L148           1 S L131 AND E287+NT
L149           0 S L131 AND E302+NT
L150           0 S L131 AND E335+NT
L151           0 S L131 AND E382+NT
                 E ALZHEIMER/CT
                 E E10+ALL
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L152          14 S L131 AND E1+NT
L153          19 S L131 AND (C2.610. OR C3.220)/CT
                 E PARKINSON/CT
                 E E5+ALL
L154           4 S L131 AND E1+NT
L155          50 S L131-L154
L156          46 S L29-L50,L89,L94,L95,L96 AND L155
                 E NICOTINIC ACETYLCHOLINE RECEPTOR/CT
                 E E3+ALL
                 E E2+ALL
L157        6649 S E19+NT
L158          27 S L155 AND L157
L159          27 S L158 AND L156
L160           4 S L155 AND CB/CT
L161           4 S L160 AND L156,L158,L159
L162          46 S L155,L156,L158,L159 NOT L161
L163           9 S L162 NOT AB/FA
L164          37 S L162 NOT L163

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 10:59:21 ON 04 MAR 2003
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FILE COVERS 1907 - 4 Mar 2003  VOL 138 ISS 10
FILE LAST UPDATED: 3 Mar 2003  (20030303/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all hitstr tot l130

L130 ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2003 ACS
AN   2002:942790  HCAPLUS
DN   138:14014
TI   Preparation of aryl olefinic amine compounds as agents for treating
     abnormal neurotransmitter release
IN   Dull, Gary Maurice; Miller, Craig Harrison; Caldwell, William Scott;
     Hadimani, Srishailkumar Basawannappa
PA   Targacept, Inc., USA
SO   U.S., 26 pp., Cont.-in-part of U.S. 6,232,316.
     CODEN: USXXAM
DT   Patent
LA   English
IC   ICM  A61K031-44
     ICS  A61K031-04; A61K031-035
NCL  514345000; 514740000; 514744000
CC   27-16 (Heterocyclic Compounds (One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 3
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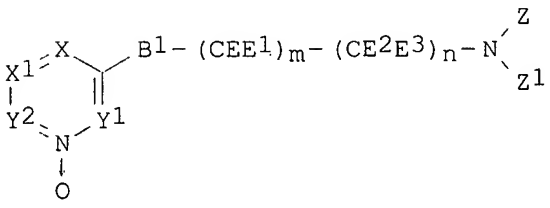
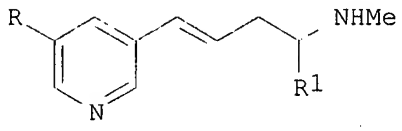
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6492399	B1	20021210	US 1999-327774	19990607
	US 6232316	B1	20010515	US 1998-98133	19980616
	WO 2000075110	A1	20001214	WO 2000-US15560	20000606
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1185514	A1	20020313	EP 2000-938183	20000606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003501416	T2	20030114	JP 2001-501591	20000606
PRAI	US 1998-98133	A2	19980616		
	US 1999-327141	A	19990607		
	US 1999-327774	A	19990607		
	WO 2000-US15560	W	20000606		
OS	MARPAT 138:14014				
GI					



I



II

AB Pharmaceutical **compns**. I (X, X1, Y, Y1, Y2 = independently C bonded to a substituent species characterized as having a .sigma.m value between -0.3 and 0.75; m + n = 1-6; B1 = 2-carbon bridging species; Z, Z1, E, E1, E2, E3 = independently H, Me) incorporate aryl substituted olefinic amine compds. and are useful for treating disorders characterized by abnormal neurotransmitter release. Representative compds. are II (R = PhCH2NHCO, NH2, Me2CHCH2O, EtS, CF3, OH; R1 = H, Me). Thus, coupling of N-methyl-N-(tert-butoxycarbonyl)-3-buten-1-amine (prepn. given) with 3-bromo-5-isobutoxypyridine (prepn. given) in the presence of Pd(OAc)2, tri-o-tolylphosphine, and Et3N gave (aminobutenyl)pyridine deriv. II (R = Me2CHCH2O, R1 = H) as its hemigalactarate salt after deprotection and salt formation. II (R = Me2CHCH2O, R1 = H) exhibits Ki = 20 nM in a **nicotinic receptor** assay, an EC50 value of 15,000 nM and an Emax value of 15% in a rubidium ion flux assay, an Emax of 6% (at a

concn. of 100 .mu.M) at muscle-type receptors, and Emax of 13% (at a concn. of 100 .mu.M) at ganglionic-type receptors.

ST aryl olefinic amine prepn neurotransmitter agent; aminobutenylpyridine prepn neurotransmitter agent; aminopentenylpyridine prepn neurotransmitter agent; pyridine aminoalkenyl prepn neurotransmitter agent; nicotonic receptor agent aminoalkenylpyridine prepn; rubidium ion release agent aminoalkenylpyridine prepn; ganglion receptor agent aminoalkenylpyridine prepn

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ganglion; prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT Nervous system agents
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT **Nicotinic receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT Neurotransmitters
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT 22537-38-8, Rubidium ion, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT 312728-27-1P 312728-36-2P 312728-41-9P 312728-44-2P 312728-50-0P 312728-55-5P 312728-56-6P 312737-86-3P 312737-87-4P 312737-88-5P 312737-90-9P 312737-91-0P 477780-47-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT 64-69-7, Iodoacetic acid 67-63-0, 2-Propanol, reactions 75-08-1, Ethanethiol 78-83-1, Isobutanol, reactions 85-41-6, Phthalimide 100-46-9, Benzylamine, reactions 526-99-8, Galactaric acid 625-31-0, 4-Penten-2-ol 625-92-3, 3,5-Dibromopyridine 626-55-1, 3-Bromopyridine 5162-44-7, 4-Bromo-1-butene 6945-68-2, 2-Amino-5-bromo-3-nitropyridine 7752-82-1, 2-Amino-5-bromopyrimidine **15585-43-0**, (E)-**Metanicotine** 20826-04-4, 5-Bromonicotinic acid 64584-92-5, (R)-4-Penten-2-ol 74115-13-2, 3-Bromo-5-hydroxypyridine 85148-26-1, 3-Chloro-5-trifluoromethylpyridine.
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)

IT 38369-88-9P, N-Methyl-3-buten-1-amine 52753-86-3P 59867-48-0P 95064-89-4P, N-Methyl-4-penten-2-amine 189274-80-4P 212332-40-6P, 3-Bromo-5-isopropoxypyridine 216689-94-0P, 3-Bromo-5-ethylthiopyridine 252870-43-2P 252870-53-4P 252870-54-5P 252870-55-6P 252870-64-7P 252870-66-9P 252870-83-0P 252870-91-0P 252870-93-2P 252870-95-4P 252870-97-6P 264228-42-4P 284040-72-8P, 3-Bromo-5-isobutoxypyridine 303031-43-8P 312728-26-0P 312728-28-2P 312728-31-7P 312728-32-8P 312728-33-9P 312728-34-0P 312728-35-1P 312728-37-3P 312728-38-4P 312728-39-5P 312728-40-8P 312728-42-0P 312728-43-1P 312728-45-3P 312728-46-4P 312728-47-5P 312728-48-6P 312728-51-1P 312728-53-3P 312728-54-4P 477780-48-6P 477780-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal

neurotransmitter release)
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; HCAPLUS
(2) Anon; HCAPLUS
(3) Anon; HCAPLUS
(4) Anon; FR 2031868 1970 HCAPLUS
(5) Anon; DE 2405930 A1 1974 HCAPLUS
(6) Anon; JP 52-134094 1977 HCAPLUS
(7) Anon; JP 54-006639 1979 HCAPLUS
(8) Anon; EP 0094080 A2 1983 HCAPLUS
(9) Anon; EP 0142057 A2 1985 HCAPLUS
(10) Anon; EP 0199845 B1 1986 HCAPLUS
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(16) Anon; EP 0559495 A1 1993 HCAPLUS
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(18) Anon; WO 9620599 1996 HCAPLUS
(19) Anon; WO 9620600 1996 HCAPLUS
(20) Anon; WO 9620929 1996 HCAPLUS
(21) Anon; WO 9631475 1996 HCAPLUS
(22) Anon; WO 9636637 1996 HCAPLUS
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(24) Anon; WO 9837071 1998 HCAPLUS
(25) Anon; WO 9845268 1998 HCAPLUS
(26) Anon; WO 9907369 1999 HCAPLUS
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(28) Anon; US 0015560 2000
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(33) Anon; CAPLUS Accession No 1991:408582
(34) Anon; CAPLUS Accession No 1992:197012
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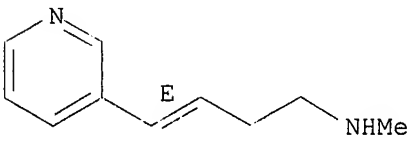
(60) Yamamoto; Agr Biol Chem, (Tokyo) V32(11), P1341 HCAPLUS
IT **15585-43-0**, (E)-**Metanicotine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aryl olefinic amine compds. as agents for treating abnormal neurotransmitter release)
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L130 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:172487 HCAPLUS
DN 136:221745
TI Irrigation solution and method for inhibition of pain and inflammation
IN Demopulos, Gregory A.; Pierce-Palmer, Pamela; Herz, Jeffrey M.
PA Omeros Medical Systems, USA
SO U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of Appl. No. PCT/US99/24625.
CODEN: USXXCO
DT **Patent**
LA English
IC ICM A61K031-4427
ICS A61K031-4439; A61K031-55
NCL 514210200
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002028798	A1	20020307	US 2001-839633	20010420
	WO 9619233	A2	19960627	WO 1995-US16028	19951212
	WO 9619233	A3	19960919		
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	US 5820583	A	19981013	US 1996-670699	19960626
	US 6261279	B1	20010717	US 1998-72913	19980504
	WO 2000023061	A2	20000427	WO 1999-US24557	19991020
	WO 2000023061	A3	20001116		
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CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
WO 2000023066 A2 20000427 WO 1999-US24672 19991020
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MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
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CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1261334 A1 20021204 EP 1999-955097 19991020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI, CY
WO 2000025745 A2 20000511 WO 1999-US26330 19991105
WO 2000025745 A3 20000824
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1994-353775 B2 19941212
WO 1995-US16028 A2 19951212
US 1996-670699 A2 19960626
US 1998-72913 A2 19980504
US 1998-105026P P 19981020
US 1998-105029P P 19981020
US 1998-105044P P 19981020
US 1998-105166P P 19981021
US 1998-107256P P 19981105
WO 1999-US24557 A2 19991020
WO 1999-US24558 A2 19991020
WO 1999-US24625 A2 19991020
WO 1999-US24672 A2 19991020
WO 1999-US26330 A2 19991105

AB A method and soln. for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The soln. preferably includes at least one pharmacol. agent selected from the group consisting of a mitogen-activated protein kinase (MAPK) inhibitor, an .alpha.2-**receptor** agonist, a neuronal **nicotinic acetylcholine receptor** agonist, a cyclooxygenase-2 (COX-2) inhibitor, a sol. **receptor** and **mixts**. thereof, and optionally addnl. multiple pain and inflammation inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. The soln. is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects assocd. with oral, i.m., s.c. or i.v. application of larger doses of the agents.

ST irrigation soln analgesic antiinflammatory
IT Tachykinin receptors
(NK1 antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Tachykinin receptors
(NK2 antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Purinoceptor antagonists
(P2X; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Bradykinin receptors
Calcitonin gene-related peptide receptors
Interleukin receptors
Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Ion channel blockers
(calcium; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Cytokine receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(class I; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT 5-HT agonists
5-HT antagonists
Analgesics
Anti-inflammatory agents
Antihistamines
Leukotriene antagonists
Nicotinic agonists
Purinoceptor agonists
Purinoceptor antagonists
Surgery
Wound
(irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Interleukin 1 receptors
Opioids
Tumor necrosis factor receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene B4, antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene D4, antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Ion channel openers
(potassium, ATP-sensitive; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sol.; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Drug delivery systems
(solns.; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
IT Blood vessel, disease
(spasm, inhibition of; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP1, antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4, antagonists; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Cytotoxic agents
(tyrphostins; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Opioids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.kappa.-; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Adrenoceptor agonists
(.alpha.2-; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Opioids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.delta.-; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT Opioids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.mu.-; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT 9029-60-1, Lipoxygenase 9043-29-2, Phospholipase A1 39391-18-9, Cyclooxygenase 142243-02-5, Mitogen-activated protein kinase 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT 9001-01-8, Kallikrein
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT 50-48-6, Amitriptyline 91-84-9, Mepyramine 146-48-5, Yohimbine 342-10-9, Kallidin 364-62-5, Metoclopramide 437-38-7, Fentanyl 1491-59-4, Oxymetazoline 4205-90-7, Clonidine 9087-70-1, Aprotinin 15307-86-5, Diclofenac 19794-93-5, Trazodone 21829-25-4, Nifedipine 33876-97-0, SIN-1 36067-72-8, BHT933 36085-73-1, BHT920 50679-08-8, Terfenadine 51803-78-2, Nimesulide 59803-98-4, UK14304 60634-51-7, LY 53857 63675-72-9, Nisoldipine 64285-06-9, (+)-Anatoxin-A 71125-38-7, Meloxicam 74103-06-3, Ketorolac 80937-31-1, Flosulide 88149-94-4, DuP 697 91147-45-4, AGN-191103 92142-32-0 100449-06-7, A-54741 103628-46-2, Sumatriptan 113563-71-6, (R)-Pinacidil 113775-47-6, Dexmedetomidine 123653-11-2, N-[2-(Cyclohexyloxy)-4-nitrophenyl]methanesulfonamide 128270-60-0, Hirulog 129623-01-4, GR82334 133052-90-1, GF 109203X 136553-81-6, BQ 123 137431-04-0, NS-49 138472-01-2, NOR-3 138614-30-9, Hoe 140 142001-63-6, SR 48968 146535-11-7, AG1296 149017-66-3, PPADS 152121-30-7 152121-47-6 152121-53-4 155262-40-1, AGN 192172 **156223-05-1**, GTS-21 158205-05-1, L-745337 158959-32-1, SC-57666 161416-43-9, A 84543 161416-98-4, A-85380 **161417-03-4**, **ABT-089** 162054-19-5 162626-99-5, FR 144420 167869-21-8 168433-84-9, SC-58451 169590-42-5, Celecoxib 179382-91-3, RS-57067 **183288-99-5**, **RJR-2403** 188627-80-7, Integrelin 189319-35-5 **198283-73-7**, **ABT-594** **203564-57-2** 340830-03-7, Receptor tyrosine kinase 402850-66-2, SBI 1765F

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

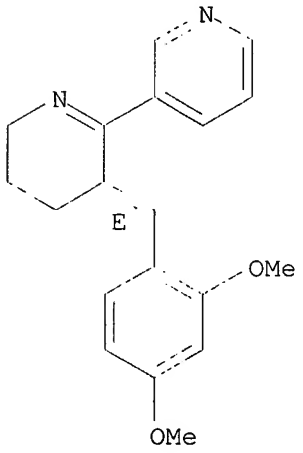
IT 168570-37-4, AGN 193080
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT 63551-76-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma., inhibitors; irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

IT **156223-05-1**, GTS-21 **161417-03-4**, **ABT-089** **183288-99-5**, **RJR-2403** **198283-73-7**, **ABT-594** **203564-57-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)

RN 156223-05-1 HCAPLUS
CN 2,3'-Bipyridine, 3-[(2,4-dimethoxyphenyl)methylene]-3,4,5,6-tetrahydro-, dihydrochloride, (3E)- (9CI) (CA INDEX NAME)

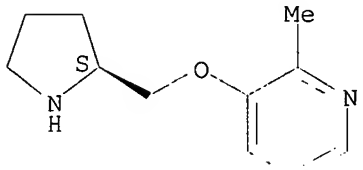
Double bond geometry as shown.



●2 HCl

RN 161417-03-4 HCAPLUS
CN Pyridine, 2-methyl-3-[(2S)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



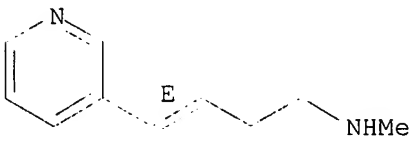
RN 183288-99-5 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2E)-2-butenedioate

(1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 15585-43-0
CMF C10 H14 N2

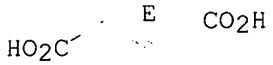
Double bond geometry as shown.



CM 2

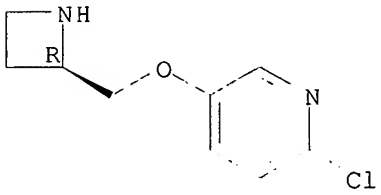
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



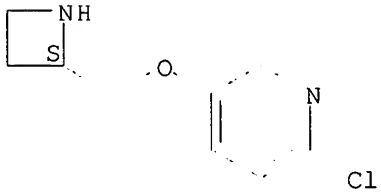
RN 198283-73-7 HCAPLUS
CN Pyridine, 5-[(2R)-2-azetidinylmethoxy]-2-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 203564-57-2 HCAPLUS
CN Pyridine, 5-[(2S)-2-azetidinylmethoxy]-2-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L130 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:71859 HCAPLUS
DN 136:112680
TI 2,3-Diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders
IN Dull, Gary Maurice

PA Targacept, Inc., USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-00
CC 1-11 (Pharmacology)
Section cross-reference(s): 27, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002005801	A2	20020124	WO 2001-US40689	20010504
WO 2002005801	A3	20020808		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-616187 A 20000714

AB Patients susceptible to or suffering from conditions and disorders, such as central nervous system disorders, are treated by administering to a patient in need thereof **compns**. that are 2,3-diacyltartaric acid salts of E-**metanicotine**. Examples are given for detn. of binding to relevant receptor sites and prepn. of (2S)-(4E)-N-methyl-5-[3-(5-isopropoxypyridin)yl]-4-penten-2-amine hemi(di-p-toluoyl-L-tartrate).

ST tartrate acyl salt **nicotine** deriv CNS disorder

IT Nervous system agents
(2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders)

IT **Nervous system**
(central, **disease**; 2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system **disorders**)

IT 2743-38-6, Dibenzoyl-L-tartaric acid 17026-42-5, Dibenzoyl-D-tartaric acid 32634-66-5, Di-p-toluoyl-L-tartaric acid 32634-68-7, Di-p-toluoyl-D-tartaric acid 50583-51-2 65259-81-6 65259-83-8 65259-84-9 76769-55-6 191605-10-4 226409-15-0 252870-53-4 391624-66-1 391624-70-7 391624-75-2 391624-77-4 391624-79-6 391624-81-0 391624-83-2 391624-84-3 391624-86-5 391624-88-7 391624-90-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders)

IT **15585-43-0**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders)

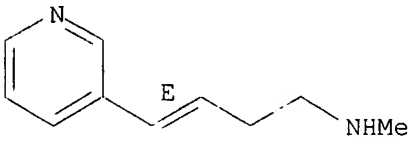
IT 391624-55-8P 391624-57-0P **391624-59-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders)

IT **15585-43-0**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders)

RN 15585-43-0 HCAPLUS

CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

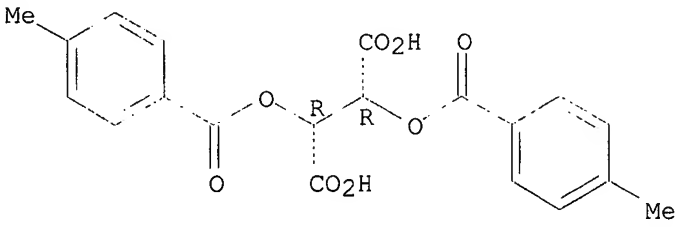


IT **391624-59-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2,3-diacyltartaric acid salts of E-**metanicotine** for treatment of central nervous system disorders)
RN 391624-59-2 HCAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (3E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 32634-66-5
CMF C20 H18 O8

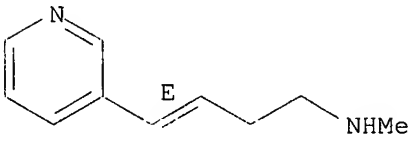
Absolute stereochemistry.



CM 2

CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



L130 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:71856 HCAPLUS
DN 136:112679
TI 2,3-Diacyltartaric acid salts of nicotinic compounds for treatment of central nervous system disorders
IN Dull, Gary Maurice; Leconte, Jean-Pierre; Kabir, Humayun
PA Targacept, Inc., USA; Aventis Pharma S.A.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT **Patent**

LA English
IC ICM A61K031-00
CC 1-11 (Pharmacology)
Section cross-reference(s): 27, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002005798	A2	20020124	WO 2001-US21872	20010711
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6432954	B1	20020813	US 2000-616743	20000714
PRAI	US 2000-616743	A	20000714		

AB Patients susceptible to or suffering from conditions and disorders, such as central nervous system disorders, are treated by administering to a patient in need thereof **compns.** that are 2,3-diacyltartaric acid salts of nicotinic compds., and particularly, nicotinic compds. that are characterized as aryl substituted amines (e.g., aryl substituted olefinic amines). Examples are give for detn. of binding to relevant receptor sites and prepn. of (2S)-(4E)-N-methyl-5-[3-(5-isopropoxypyridin)yl]-4-penten-2-amine hemi(di-p-toluoyl-L-tartrate).

ST tartrate acyl salt nicotinic acid deriv CNS disorder

IT Nervous system agents
(2,3-diacyltartaric acid salts of nicotinic compds. for treatment of central nervous system disorders)

IT **Nervous system**
(central, **disease**; 2,3-diacyltartaric acid salts of nicotinic compds. for treatment of central nervous system **disorders**)

IT 2743-38-6, Dibenzoyl-L-tartaric acid 17026-42-5, Dibenzoyl-D-tartaric acid 32634-66-5, Di-p-toluoyl-L-tartaric acid 32634-68-7, Di-p-toluoyl-D-tartaric acid 50583-51-2 65259-81-6 65259-83-8 65259-84-9 76769-55-6 191605-10-4 226409-15-0 252870-53-4 391624-66-1 391624-70-7 391624-75-2 391624-77-4 391624-79-6 391624-81-0 391624-83-2 391624-84-3 391624-86-5 391624-88-7 391624-90-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(2,3-diacyltartaric acid salts of nicotinic compds. for treatment of central nervous system disorders)

IT 391624-55-8P 391624-57-0P **391624-59-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2,3-diacyltartaric acid salts of nicotinic compds. for treatment of central nervous system disorders)

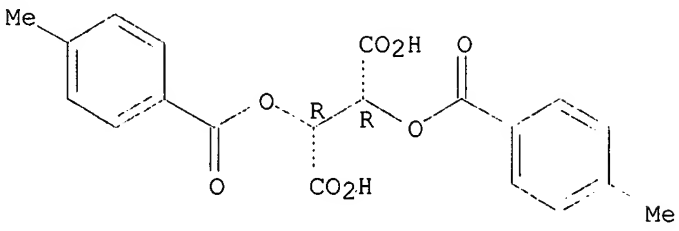
IT **391624-59-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2,3-diacyltartaric acid salts of nicotinic compds. for treatment of central nervous system disorders)

RN 391624-59-2 HCAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (3E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 32634-66-5
CMF C20 H18 O8

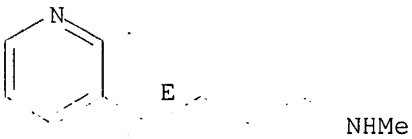
Absolute stereochemistry.



CM 2

CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



L130 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:850927 HCAPLUS
DN 135:376774
TI Method of treating vaginal dryness with **nicotinic acetylcholine receptor** agonists
IN Yerxa, Benjamin R.
PA Inspire Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087288	A2	20011122	WO 2001-US40714	20010509
	WO 2001087288	C1	20020829		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6448276	B1	20020910	US 2000-574831	20000517
	EP 1253916	A1	20021106	EP 2001-935773	20010509
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-574831	A	20000517		
	WO 2001-US40714	W	20010509		

OS MARPAT 135:376774

AB The invention provides a method for treating vaginal dryness by increasing hydration and lubrication of vaginal and cervical tissues in a subject in need of such treatment. The method **comprises** administering to the subject a **nicotinic acetylcholine receptor** agonist such as **nicotine** and its analogs, trans-**metanicotine** and its analogs, **epibatidine** and its analogs, lobeline and its analogs, pyridol derivs., p-alkylthiophenol derivs., and imidacloprid and its analogs, in an amt. effective to stimulate cervical and vaginal secretions. Pharmaceutical **formulations** and methods of making the same are also disclosed. Methods of administering the **formulation** include: topical administration via a liq., gel, cream, ointment, foam, pessary, or tablet; systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liq. or pill), injectable, suppository form, or transdermal form. The invention is useful for treating vaginal dryness and vulvar pain.

ST **nicotinic receptor** agonist vaginal dryness; oral topical parenteral **nicotinic receptor** agonist

IT Uterus
(cervix, hydration and lubrication of; method of treating vaginal dryness with **nicotinic acetylcholine receptor** agonists)

IT Nicotinic agonists
(**compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Hydration, physiological
(enhancement of; method of treating vaginal dryness with **nicotinic acetylcholine receptor** agonists)

IT Drug delivery systems
(foams; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(gels; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Vagina
(hydration and lubrication of; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(inhalants; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(injections; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(liqs., oral; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(nasal sprays; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(ointments, creams; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

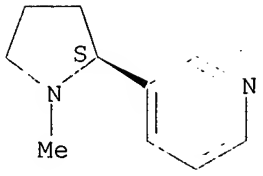
IT Drug delivery systems
(ointments; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Drug delivery systems
(oral; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)

IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperidine; **compns**. contg. nicotinic agonists for treatment

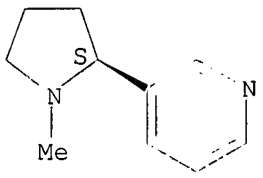
of vaginal dryness)
IT Mucins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(secretion; method of treating vaginal dryness with **nicotinic acetylcholine receptor** agonists)
IT Drug delivery systems
(solns., nasal; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(solns., topical; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(suppositories; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(suspensions; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(tablets; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(topical; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(transdermal; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Drug delivery systems
(vaginal, pessaries; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Analgesics
(vulvar; **compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT Pain
(vulvar; method of treating vaginal dryness with **nicotinic acetylcholine receptor** agonists)
IT **54-11-5, Nicotine 54-11-5D, Nicotine**
, analogs 90-69-7, Lobeline 90-69-7D, Lobeline, analogs 108-98-5D, Thiophenol, p-alkyl derivs. **15585-43-0**, trans-**Metanicotine 15585-43-0D**, trans-**Metanicotine**, analogs 138261-41-3, Imidacloprid 138261-41-3D, Imidacloprid, analogs **140111-52-0, Epibatidine 140111-52-0D, Epibatidine**, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns**. contg. nicotinic agonists for treatment of vaginal dryness)
IT **54-11-5, Nicotine 54-11-5D, Nicotine**
, analogs **15585-43-0**, trans-**Metanicotine 15585-43-0D**, trans-**Metanicotine**, analogs **140111-52-0, Epibatidine 140111-52-0D, Epibatidine**, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**compns**. contg. nicotinic agonists for treatment of vaginal dryness)
RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



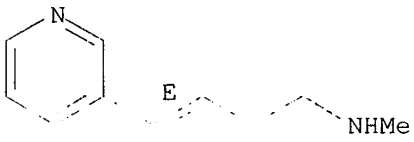
RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



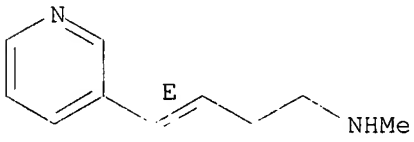
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



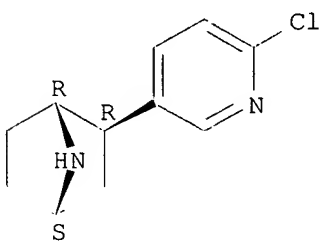
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 140111-52-0 HCAPLUS
CN 7-Azabicyclo[2.2.1]heptane, 2-(6-chloro-3-pyridinyl)-, (1R,2R,4S)- (9CI) (CA INDEX NAME)

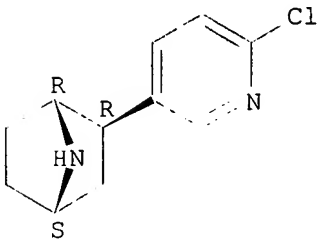
Absolute stereochemistry.



RN 140111-52-0 HCAPLUS

CN 7-Azabicyclo[2.2.1]heptane, 2-(6-chloro-3-pyridinyl)-, (1R,2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



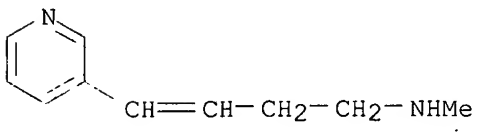
L130 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:816502 HCAPLUS
DN 135:340964
TI Imaging of **nicotinic acetylcholine receptor subtypes**
IN Bencherif, Merouane; Miller, Craig Harrison; Dull, Gary Maurice; Bhatti, Balwinder Singh; Caldwell, William Scott
PA Targacept, Inc., USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K051-04
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001082978	A2	20011108	WO 2001-US13950	20010501
WO 2001082978	A3	20020801		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-562485 A 20000501
AB Compds. useful as probes for detg. the relative no. and/or function of specific receptor subtypes are claimed. Of particular interest are **nicotinic** agonists and antagonists (e.g., **metanicotine** -type compds. and azaadamantane-type compds.) that are selective to certain **nicotinic receptor subtypes**. Those compds. are labeled with a radioactive isotopic moiety such as 11C, 18F, 76Br, 123I or 125I. Central nervous system disorders are diagnosed by administering to a patient a detectably labeled compd., and detecting the binding of that compd. to selected **nicotinic receptor subtypes** (e.g., alpha 7 and/or alpha 4 beta 2 **receptor subtypes**). The compds. that have been administered are detected using methods such as position emission topog. (PET) and single-photon emission computed tomog. (SPECT). The present invention is useful in the diagnosis of a wide variety of CNS diseases and disorders, including **Alzheimer**'s disease, **Parkinson**'s disease and **schizophrenia**.

ST CNS disorder imaging **nicotinic acetylcholine receptor**
IT **Nervous system**
(central, **disease**; imaging of **nicotinic acetylcholine receptor subtypes**)
IT **Alzheimer's disease**
Diagnosis
Nicotinic agonists
Nicotinic antagonists
Parkinson's disease
Positron-emission tomography
Radiopharmaceuticals
Schizophrenia
Single-photon-emission computed tomography
(imaging of **nicotinic acetylcholine receptor subtypes**)
IT **Nicotinic receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(imaging of **nicotinic acetylcholine receptor subtypes**)
IT 242126-46-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(imaging of **nicotinic acetylcholine receptor subtypes**)
IT 242126-39-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(imaging of **nicotinic acetylcholine receptor subtypes**)
IT 281-23-2D, Adamantane, aza analogs **538-79-4D**, **Metanicotine**, analogs 13981-56-1D, Fluorine 18, ligands labeled with, biological studies 14158-31-7D, Iodine 125, ligands labeled with, biological studies 14333-33-6D, Carbon 11, ligands labeled with, biological studies 15715-08-9D, Iodine 123, ligands labeled with, biological studies 15765-38-5D, Bromine 76, ligands labeled with, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imaging of **nicotinic acetylcholine receptor subtypes**)
IT **538-79-4D**, **Metanicotine**, analogs
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imaging of **nicotinic acetylcholine receptor subtypes**)
RN 538-79-4 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



L130 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:611752 HCAPLUS
DN 135:175425
TI Method of treating dry eye disease with **nicotinic acetylcholine receptor** agonists
IN Yerxa, Benjamin R.
PA Inspire Pharmaceuticals, Inc., USA
SO U.S., 9 pp.

CODEN: USXXAM
DT **Patent**
LA English
IC ICM A61K031-505
ICS A61K031-44
NCL 514256000
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6277855	B1	20010821	US 2000-557059	20000421
	WO 2001080844	A2	20011101	WO 2001-US13034	20010419
	WO 2001080844	A3	20020328		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1214062	A2	20020619	EP 2001-927298	20010419
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-557059	A	20000421		
	WO 2001-US13034	W	20010419		

OS MARPAT 135:175425

AB The invention provides a method for increasing hydration and lubrication of lacrimal tissues in a subject in need of such treatment. The method **comprises** administering to the subject a **nicotinic acetylcholine receptor** agonist such as **nicotine** and its analogs, transmetanicotine and its analogs, epibatidine and it analogs, lobeline and its analogs, pyridol derivs., para-alkylthiophenol derivs., and imidacloprid and its analogs, in an amt. effective to stimulate mucus secretion in the lacrimal system. Pharmaceutical **formulations** and methods of making the same are also disclosed. Methods of administering the **formulation** include: topical administration via a liq., gel, cream, or as part of a contact lens or selective release membrane; or systemic administration via nasal drops or spray, inhalation by nebulizer or other device, oral form (liq. or pill), injectable, intra-operative instillation, suppository form, or transdermal form. The invention is useful for treating dry eye disease and corneal injury.

ST dry eye disease **nicotinic acetylcholine receptor** agonist; cornea injury treatment nicotinic agonist

IT Medical goods
(catheters; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)

IT Drug delivery systems
(chewing gums; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)

IT Drug delivery systems
(contact lens; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)

IT Eye, disease
(cornea, injury; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)

IT Drug delivery systems
(drops; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)

IT Eye, disease

(dry; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(foams; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(gels, topical; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(gels; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Lacrimal gland
(increasing hydration and lubrication of; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(infusion pumps; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(infusions; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(inhalants, nebularized liqs.; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(liposomes, topical; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(liposomes; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(liqs.; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(nasal sprays; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Contact lenses
Drug delivery systems
Hydration, physiological
Lubrication
Nicotinic agonists
Sjogren's syndrome
(**nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(ointments, creams; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(ointments; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(ophthalmic; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(oral; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Alkaloids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperidine; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)

IT Drug delivery systems
(powders; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(solns., nasal; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(sprays; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Mucins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(stimulation of mucosal goblet cells release of; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(suppositories; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(suspensions; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(sustained-release; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(topical; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT Drug delivery systems
(transdermal; **nicotinic acetylcholine receptor** agonists for treating dry eye disease)
IT **54-11-5, Nicotine 54-11-5D, Nicotine**, analogs 90-69-7, Lobeline 90-69-7D, Lobeline, analogs 108-98-5D, Thiophenol, p-alkyl derivs. **15585-43-0**, Trans-**Metanicotine 15585-43-0D**, Trans-**Metanicotine**, analogs 138261-41-3, Imidacloprid 138261-41-3D, Imidacloprid, analogs **140111-52-0, Epibatidine 140111-52-0D, Epibatidine**, analogs **355114-70-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nicotinic acetylcholine receptor** agonists for treating dry eye disease)
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WO 9746554 1997 HCAPLUS
(2) Anon; WO 9834593 1998 HCAPLUS
(3) Badio; Eur J Pharmacol 1997, V321, P189 HCAPLUS
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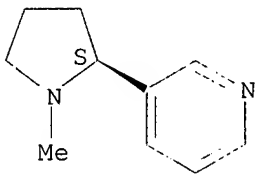
IT **54-11-5, Nicotine 54-11-5D, Nicotine**
, analogs **15585-43-0**, Trans-**Metanicotine**
15585-43-0D, Trans-**Metanicotine**, analogs
140111-52-0, Epibatidine 140111-52-0D,
Epibatidine, analogs **355114-70-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nicotinic acetylcholine receptor**
agonists for treating dry eye disease)

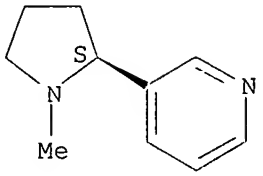
RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



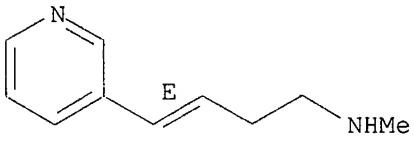
RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



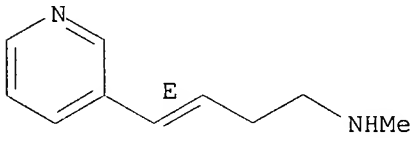
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



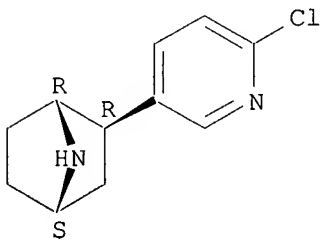
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



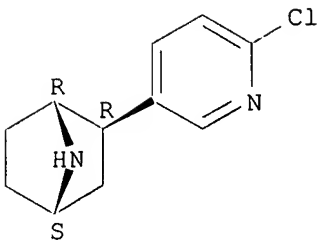
RN 140111-52-0 HCAPLUS
CN 7-Azabicyclo[2.2.1]heptane, 2-(6-chloro-3-pyridinyl)-, (1R,2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 140111-52-0 HCAPLUS
CN 7-Azabicyclo[2.2.1]heptane, 2-(6-chloro-3-pyridinyl)-, (1R,2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

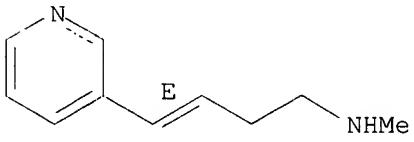


RN 355114-70-4 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 15585-43-0
CMF C10 H14 N2

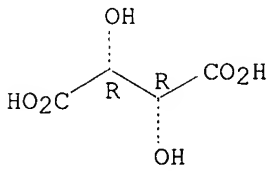
Double bond geometry as shown.



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



L130 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:881121 HCAPLUS
DN 134:42065
TI Preparation of aryl substituted olefinic amines as nicotinic cholinergic receptor agonists
IN Dull, Maurice Dull; Miller, Craig Harrison; Caldwell, William Scott; Lynm, Dwo; Bhatti, Balwinder Singh; Schmitt, Jeffrey Daniel; Byrd, Gary Dwight; Hadimani, Srishailkumar Basawannappa
PA Targacept, Inc., USA
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C07D213-74
ICS C07D213-82; C07D213-65; C07D213-70; C07D213-26; C07D213-89; A61K031-44; A61K031-505

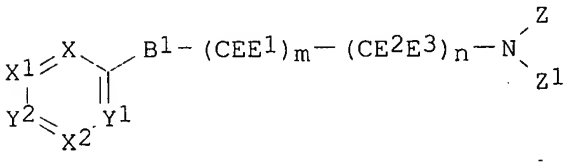
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000075110	A1	20001214	WO 2000-US15560	20000606
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6492399	B1	20021210	US 1999-327774	19990607
	US 6455554	B1	20020924	US 2000-570226	20000512
	EP 1185514	A1	20020313	EP 2000-938183	20000606
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003501416	T2	20030114	JP 2001-501591	20000606
PRAI	US 1999-327141	A	19990607		
	US 1999-327774	A	19990607		
	US 1998-98133	A2	19980616		
	WO 2000-US15560	W	20000606		

OS MARPAT 134:42065

GI



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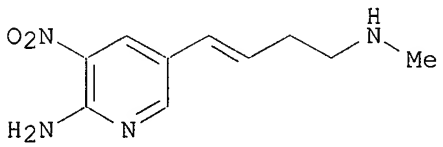

II

AB The title compds. (I) [wherein X, X1, X2, Y1, and Y2 = independently N, N(:O), or substituted C; < 3 of X, X1, X2, Y1, and Y2 = N or N(:O) and .ltoreq. 1 of X, X1, X2, Y1, and Y2 = N(:O); m + n = 1-6; B1 = 2-carbon bridging group; Z, Z1, E, E1, E2, and E3 = independently = H or Me] were prepd. and the compds. tested for the treatment of central nervous system (CNS) disorders. For example, amination of 4-bromo-1-butene with Me-NH2 (57.6%), followed by N-protection with benzoyl chloride (56.3%), Pd-catalyzed coupling of the olefin with 2-amino-5-bromo-3-nitropyridine (51.7%), and deprotection (66.7%) afforded (3E)-N-methyl-4-(5-nitro-6-aminopyridin-3-yl)-3-buten-1-amine (II). II exhibited good high affinity binding to certain CNS **nicotinic receptors** with Ki of 3 nM. It exhibited an Emax value of 0% for dopamine release relative to (S)-(-)-**nicotine**, indicating selectivity in eliciting neurotransmitter release. In the rubidium ion flux assay, II gave an EC50 value of 26,000 nM and an Emax value of 22%. Neurotransmitter release

from rat brain synaptosomes in the presence of II was measured as an Emax value of 33%. Finally, II exhibited Emax values of 10% and 11% at concns. of 100 .mu.M for muscle-type and ganglionic-type receptors, resp. Thus, I provide a therapeutic window for utilization in the treatment of CNS disorders without undesirable side effects.

ST aryl substituted olefinic amine prepn nicotinic cholinergic receptor agonist; pyridylbutenamine pyridylpentenamine prepn central nervous system disorder treatment

IT Nervous system agents
Nicotinic agonists
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

IT **Nicotinic receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

IT 312728-32-8P 312728-33-9P 312728-38-4P 312728-46-4P 312728-53-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

IT 312728-27-1P 312728-30-6P 312728-36-2P 312728-41-9P 312728-44-2P
312728-49-7P 312728-50-0P 312728-55-5P 312728-56-6P 312737-86-3P
312737-87-4P 312737-88-5P 312737-90-9P 312737-91-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

IT 51-61-6, Dopamine, biological studies **54-11-5, Nicotine**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

IT 85-41-6, Phthalimide 144-62-7, Oxalic acid, reactions 526-99-8, Galactaric acid 617-89-0, Furfurylamine 625-31-0, 4-Penten-2-ol 625-92-3, 3,5-Dibromopyridine 626-55-1, 3-Bromopyridine 5162-44-7, 4-Bromo-1-butene 6945-68-2, 2-Amino-5-bromo-3-nitropyridine 7752-82-1, 2-Amino-5-bromopyrimidine 15448-47-2, (R)-(+)-Propylene oxide, reactions **15585-43-0**, (3E)-N-Methyl-4-(3-pyridinyl)-3-buten-1-amine 20826-04-4, 5-Bromonicotinic acid 85148-26-1, 3-Chloro-5-trifluoromethylpyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

IT 38369-88-9P, N-Methyl-3-buten-1-amine 52753-86-3P, 4-Penten-2-ol p-Toluenesulfonate 59867-48-0P 64584-92-5P 74115-13-2P, 3-Bromo-5-hydroxypyridine 95064-89-4P, N-Methyl-4-penten-2-amine 189274-80-4P, (4E)-N-Methyl-5-(3-pyridyl)-4-penten-2-amine 212332-40-6P, 5-Bromo-3-isopropoxypyridine 216689-94-0P, 3-Bromo-5-ethylthiopyridine 252870-43-2P 252870-53-4P 252870-54-5P 252870-55-6P 252870-64-7P, (4E)-5-(3-Pyridyl)-4-penten-2-ol 252870-66-9P, (4E)-5-(3-Pyridyl)-4-penten-2-ol p-Toluenesulfonate 252870-83-0P, N-Methyl-N-(tert-butoxycarbonyl)-4-penten-2-amine 252870-91-0P 252870-93-2P

252870-95-4P 252870-97-6P 264228-42-4P, N-Methyl-N-(3-buten-1-yl)benzamide 284040-72-8P, 3-Bromo-5-isobutoxypyridine 303031-43-8P 312728-26-0P 312728-28-2P, N-Methyl-N-(tert-butoxycarbonyl)-3-buten-1-amine 312728-29-3P 312728-31-7P 312728-34-0P 312728-35-1P 312728-37-3P 312728-39-5P, (3E)-N-Methyl-N-(tert-butoxycarbonyl)-4-(3-pyridinyl)-3-buten-1-amine 312728-40-8P 312728-42-0P, (4E)-N-Methyl-N-(tert-butoxycarbonyl)-5-(3-pyridyl)-4-penten-2-amine 312728-43-1P 312728-45-3P 312728-47-5P 312728-48-6P 312728-51-1P 312728-52-2P 312728-54-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Anon; US 5663356 A 1997 HCAPLUS
(3) Bencherif, M; WO 9620600 A 1996 HCAPLUS
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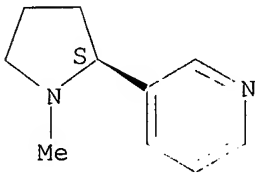
(43) Yamamoto, I; Agr Biol Chem 1968, V32(11), P1341 HCAPLUS

IT **54-11-5, Nicotine**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic

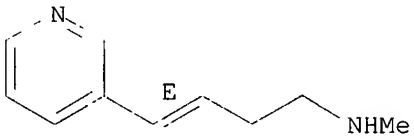
receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)
RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **15585-43-0**, (3E)-N-Methyl-4-(3-pyridinyl)-3-buten-1-amine
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aryl substituted olefinic amine nicotinic cholinergic receptor agonists by Pd-catalyzed coupling of olefins with aryl halides)
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L130 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:756513 HCAPLUS
DN 133:317546
TI Pharmaceutical compositions for inhibition of cytokine production and secretion
IN Bencherif, Merouane
PA Targacept, Inc., USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-00
CC 1-7 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000062767	A2	20001026	WO 2000-US10551	20000420
WO 2000062767	A3	20010308		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6166048	A	20001226	US 1999-295181	19990420
EP 1171127	A2	20020116	EP 2000-926142	20000420

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

	BR 2000009869	A	20020326	BR 2000-9869	20000420
	JP 2002542188	T2	20021210	JP 2000-611904	20000420
	US 6489349	B1	20021203	US 2000-656284	20000906
PRAI	US 1999-295181	A	19990420		
	US 1996-631761	B2	19960423		
	WO 2000-US10551	W	20000420		

OS MARPAT 133:317546

AB Pharmaceutical compns. contg. compds. that affect cytokine prodn. and/or secretion, such as aryl substituted olefinic amine compds., pyridyloxylalkylamines and phenoxyalkylamines, and aryl substituted amine compds., such as 3-aminophenyl amine compds. are described. The compns. are useful for the prevention or treatment of conditions, diseases and disorders assocd. with dysfunction, e.g., undesirably high levels of cytokine prodn. and/or secretion, such as inflammatory bowel disease, inflammation, arthritis, cachexia in neoplastic diseases or assocd. with AIDS, and autoimmune diseases. The compds. of the present invention, in the therapeutic amts. used, do not cause any appreciable effects at muscle and ganglionic sites, thus indicating a lack of undesirable side effects of those compds. Cytokine inhibition was evaluated in human monocytic leukemia cells (MonoMac 6 cells) and human erythroleukemia bone marrow cells (TF-1 cells); ED50 and Emax for (Z)-**metanicotine** monofumarate were 100 nM and 100%, and for (E)-4-[3-(5-methoxypyridin)yl]-3-buten-1-amine monofumarate were 0.2 nM and 100%, resp.

ST amine cytokine inflammation cachexia autoimmune disease

IT Cachexia
(assocd. with AIDS; compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

IT Cachexia
(cancerous; compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

IT AIDS (disease)
Anti-AIDS agents
Anti-inflammatory agents
Antiarthritics
Autoimmune disease
Drug delivery systems
(compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

IT Cytokines
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

IT Amines, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

IT **1129-68-6 15585-43-0** 112086-55-2 119981-51-0
132424-10-3 180740-78-7 **180915-55-3** 189274-80-4
198976-88-4 198976-89-5 198976-90-8 198976-91-9 198976-92-0
198976-93-1 198976-94-2 198976-95-3 198976-96-4 198976-97-5
198976-98-6 198976-99-7 198977-00-3 198977-01-4 198977-02-5
198977-03-6 198977-04-7 198977-07-0 198977-08-1 198977-09-2
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198977-25-2 198977-26-3 198977-27-4 198977-28-5 198977-29-6
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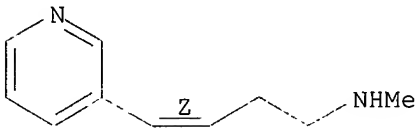
198977-39-8 198977-40-1 198977-41-2 212332-31-5 212332-33-7
246137-85-9 246137-86-0 303104-02-1 303104-59-8 303104-61-2
303104-63-4 303104-65-6 303104-67-8 303104-69-0 303104-71-4
303104-74-7 303104-76-9 303104-80-5 303104-82-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

IT **1129-68-6 15585-43-0 180915-55-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. alkyl and aryl substituted amines for inhibition of cytokine prodn. and secretion)

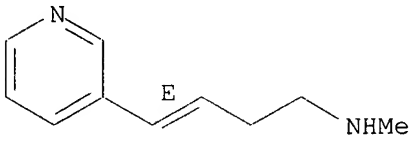
RN 1129-68-6 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

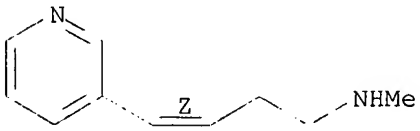


RN 180915-55-3 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 1129-68-6
CMF C10 H14 N2

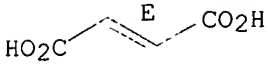
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



L130 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:553442 HCAPLUS
DN 133:168383
TI Pharmaceutical **compositions** containing **nicotine** or a ligand of **nicotine receptors** and a monamine oxidase inhibitor and their use for treating **tobacco withdrawal** symptoms
IN Caille, Dominique; George, Pascal; Jegham, Samir; Robineau, Pascale; Scatton, Bernard; Zivkovic, Branimir
PA Sanofi-Synthelabo, Fr.
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT **Patent**
LA French
IC ICM A61K045-06
ICS A61K031-535; A61K031-465; A61K031-42
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

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PI	WO 2000045846	A1	20000810	WO 2000-FR193	20000128
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2788982	A1	20000804	FR 1999-1144	19990202
	FR 2788982	B1	20020802		
	EP 1150715	A1	20011107	EP 2000-901660	20000128
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002536342	T2	20021029	JP 2000-596965	20000128
PRAI	FR 1999-1144	A	19990202		
	WO 2000-FR193	W	20000128		

OS MARPAT 133:168383
AB The invention concerns novel pharmaceutical **compns**. contg. **nicotine** or a ligand of **nicotine receptors** and a monamine oxidase inhibitor designed for treating **tobacco withdrawal** symptoms. A bilayer tablet contained befloxatone 5, lactose 66, microcryst. cellulose 20, povidone 4, crospovidone 4, and magnesium stearate 1% in the first layer, and **nicotine** polacrylix 5, microcryst. cellulose 20 povidone 4, hydroxypropyl Me cellulose 25, magnesium stearate 1, and lactose q.s. 100% in the second layer.
ST pharmaceutical **nicotine** receptor monamine oxidase inhibitor; **tobacco withdrawal** symptom tablet befloxatone **nicotine**
IT **Drug** delivery systems
(capsules; pharmaceutical **compns**. contg. **nicotine** or ligand of **nicotine receptors** and monamine oxidase inhibitor and their use for treating **tobacco**

withdrawal symptoms)
IT Drug delivery systems
(chewing gums; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(inhalants; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(injections; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(nasal; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(oral; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(parenterals; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Nicotinic receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(suppositories; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(tablets; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(tapes; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT Drug delivery systems
(transdermal; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine oxidase inhibitor and their use for treating tobacco withdrawal symptoms)
IT 9001-66-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; pharmaceutical compns. contg. nicotine or ligand of nicotine receptors and monamine

oxidase inhibitor and their use for treating **tobacco withdrawal** symptoms)

IT **54-11-5, Nicotine** 90-69-7, Lobelin 262-20-4, Phenoxathiin 357-70-0, Galantamine 485-35-8, Cytisine **538-79-4, Metanicotine** 555-57-7, Pargyline 14611-51-9, L-Deprenyl 18464-39-6, Caroxazone 29218-27-7, Toloxatone 60762-57-4, Pirlindole 63638-91-5, Brofaromine 64840-90-0, Eperisone 71320-77-9, Moclobemide 75603-31-5, An 072 76990-56-2, Milacemide 77518-07-1, Amiflamine 91406-11-0, Esuprone 93438-65-4, Conantokin g 94011-82-2, Bazinaprine 103878-84-8, Lazabemide 105365-76-2, Rs8359 117854-28-1, Befol 119386-96-8, Mofegiline 134564-82-2, Befloxatone 135204-83-0, t794 136236-51-6, Rasagiline **140111-52-0, Epibatidine 147402-53-7, Abt-418** 150366-18-0, e 2011 156137-99-4, Rapacuronium bromide **156223-05-1**, Gts-21 161416-98-4, a 85380 **161417-03-4, Abt 089** 164523-00-6 176773-68-5 176773-86-7 178419-47-1, AR-R 17779 **179120-92-4, Altinicline 183288-99-5, Rjr 2403** 189439-39-2 189439-83-6 189439-84-7 190733-42-7 190733-47-2 190733-50-7 190789-14-1 190789-52-7 **191611-76-4, Sib 1553a** 195211-53-1, Dbo 83 **198283-73-7, Abt 594** 205187-44-6, KP 9 207391-08-0 207391-13-7 207391-21-7 207391-34-2 207391-48-8 207391-53-5 214189-84-1 214189-85-2 214901-35-6 215367-30-9 215367-49-0 215367-62-7 215367-72-9 216579-65-6 216579-73-6 216580-87-9 216581-23-6 216581-38-3 216853-05-3 216853-29-1 216853-36-0 216970-31-9 216970-32-0 216970-33-1 220100-50-5 223795-00-4 223796-26-7 223796-36-9 223796-52-9 223797-21-5 223797-32-8 224818-46-6 287973-22-2 287973-23-3 287973-24-4 287973-25-5 287973-26-6 287973-27-7 287973-28-8 287973-29-9 287973-30-2 287973-31-3 287973-32-4 287973-33-5 287980-51-2, GW 280430 287980-52-3, RJR 2531 287980-53-4, RJR 2557
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **compns.** contg. **nicotine** or ligand of **nicotine receptors** and monamine oxidase inhibitor and their use for treating **tobacco withdrawal** symptoms)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

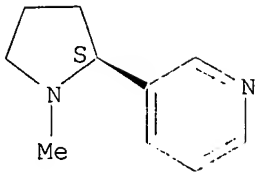
RE

(1) Cinciripini, P; ONCOLOGY 1998
(2) La Roche, H; WO 9528934 A 1995 HCAPLUS
(3) Williams, J; US 5803081 A 1998 HCAPLUS

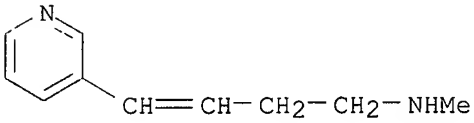
IT **54-11-5, Nicotine 538-79-4, Metanicotine 140111-52-0, Epibatidine 147402-53-7, Abt-418 156223-05-1,** Gts-21 **161417-03-4, Abt 089 179120-92-4, Altinicline 183288-99-5, Rjr 2403 191611-76-4, Sib 1553a 198283-73-7, Abt 594**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical **compns.** contg. **nicotine** or ligand of **nicotine receptors** and monamine oxidase inhibitor and their use for treating **tobacco withdrawal** symptoms)

RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

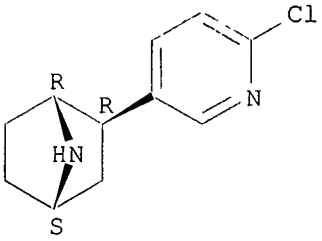


RN 538-79-4 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



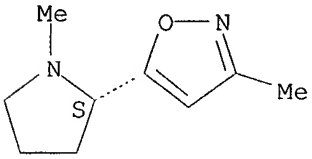
RN 140111-52-0 HCAPLUS
CN 7-Azabicyclo[2.2.1]heptane, 2-(6-chloro-3-pyridinyl)-, (1R,2R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



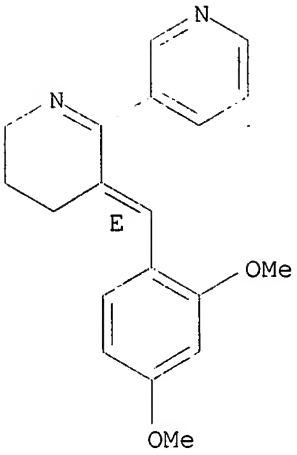
RN 147402-53-7 HCAPLUS
CN Isoxazole, 3-methyl-5-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 156223-05-1 HCAPLUS
CN 2,3'-Bipyridine, 3-[(2,4-dimethoxyphenyl)methylene]-3,4,5,6-tetrahydro-, dihydrochloride, (3E)- (9CI) (CA INDEX NAME)

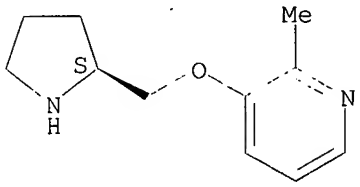
Double bond geometry as shown.



●2 HCl

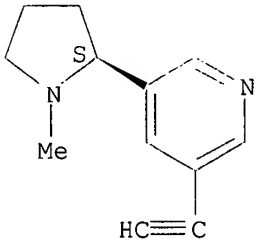
RN 161417-03-4 HCAPLUS
CN Pyridine, 2-methyl-3-[(2S)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 179120-92-4 HCAPLUS
CN Pyridine, 3-ethynyl-5-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

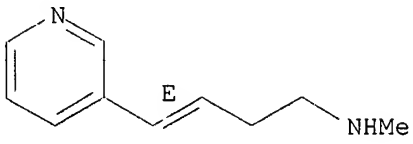


RN 183288-99-5 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 15585-43-0
CMF C10 H14 N2

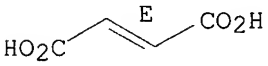
Double bond geometry as shown.



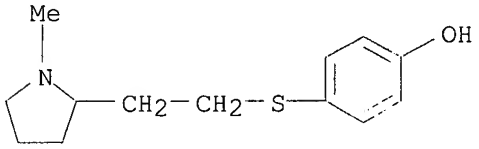
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

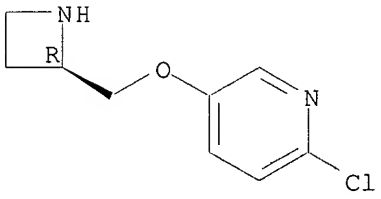


RN 191611-76-4 HCAPLUS
CN Phenol, 4-[[2-(1-methyl-2-pyrrolidinyl)ethyl]thio]- (9CI) (CA INDEX NAME)



RN 198283-73-7 HCAPLUS
CN Pyridine, 5-[(2R)-2-azetidinylmethoxy]-2-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L130 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:277840 HCAPLUS
DN 132:313697
TI Irrigation solution for inhibition of pain and inflammation
IN Demopulos, Gregory A.; Palmer, Pamela P.; Herz, Jeffrey M.
PA Omeros Medical Systems, Inc., USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 13
FAN.CNT 9

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2000023062 A2 20000427 WO 1999-US24558 19991020
WO 2000023062 A3 20000727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2002028798 A1 20020307 US 2001-839633 20010420
PRAI US 1998-105044P P 19981020
US 1994-353775 B2 19941212
WO 1995-US16028 A2 19951212
US 1996-670699 A2 19960626
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US 1998-105026P P 19981020
US 1998-105029P P 19981020
US 1998-105166P P 19981021
US 1998-107256P P 19981105
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WO 1999-US24672 A2 19991020
WO 1999-US26330 A2 19991105

AB A method and soln. for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The soln. preferably includes at least 1 neuronal **nicotinic acetylcholine receptor** agonist and, optionally, addnl. multiple pain and inflammation inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. The soln. is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects assocd. with oral, i.m., s.c. or i.v. application of larger doses of the agents. One preferred soln. to inhibit pain and inflammation includes a neuronal **nicotinic acetylcholine receptor** agonist, serotonin **receptor**-2 and serotonin **receptor**-3 antagonists, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, neurokinin **receptor**-1 and neurokinin **receptor**-2 antagonists, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, calcium channel, bradykinin **receptor**-1 and bradykinin **receptor**-2 antagonists, and a .mu.-opioid agonist. Thus, an irrigation soln. for cardiovascular and general vascular therapeutic and diagnostic procedures consists of a serotonin receptor-2 antagonist, LY-53857 50 nM.

ST irrigation soln inhibition pain; inflammation inhibition irrigation soln; serotonin antagonist irrigation soln

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ATP-sensitive; irrigation soln. for inhibition of pain and inflammation)

IT Purinoceptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (P2X, agonists; irrigation soln. for inhibition of pain and inflammation)

IT Purinoceptor antagonists
(P2X; irrigation soln. for inhibition of pain and inflammation)

IT Purinoceptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (P2Y, agonists; irrigation soln. for inhibition of pain and inflammation)

IT Bradykinin receptors
Calcitonin gene-related peptide receptors
Interleukin receptors
Prostanoid receptors
Tachykinin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; irrigation soln. for inhibition of pain and inflammation)
IT Drug delivery systems
(injections, i.v.; irrigation soln. for inhibition of pain and inflammation)
IT 5-HT agonists
5-HT antagonists
Analgesics
Anti-inflammatory agents
Antihistamines
Opioid antagonists
Purinoceptor agonists
Purinoceptor antagonists
Thromboxane receptor antagonists
Wound healing
(irrigation soln. for inhibition of pain and inflammation)
IT Cholinergic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(irrigation soln. for inhibition of pain and inflammation)
IT Leukotriene antagonists
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)
IT Opioids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)
IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene B4, antagonists; irrigation soln. for inhibition of pain and inflammation)
IT Leukotriene receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(leukotriene D4, antagonists; irrigation soln. for inhibition of pain and inflammation)
IT Eicosanoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor antagonists; irrigation soln. for inhibition of pain and inflammation)
IT Drug delivery systems
(solns.; irrigation soln. for inhibition of pain and inflammation)
IT Opioid receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.kappa.-opioid, agonists; irrigation soln. for inhibition of pain and inflammation)
IT Opioid receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.delta.-opioid, agonists; irrigation soln. for inhibition of pain and inflammation)
IT Opioid receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.mu.-opioid, agonists; irrigation soln. for inhibition of pain and inflammation)
IT 9001-01-8, Kallikrein 9013-93-8, Phospholipase 9029-60-1, Lipoxygenase
39391-18-9, Cyclooxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; irrigation soln. for inhibition of pain and inflammation)
IT 50-48-6 59-33-6, Mepyramine 146-48-5, Yohimbine 364-62-5,
Metoclopramide 437-38-7, Fentanyl 2826-26-8 9087-70-1, Aprotinin
19794-93-5, Trazodone 21829-25-4, Nifedipine 33876-97-0, SIN-1

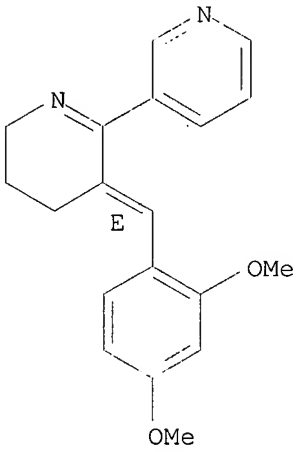
50679-08-8, Terfenadine 60634-51-7, LY 53857 63675-72-9, Nisoldipine 71800-37-8 74103-06-3, Ketorolac 92454-60-9, FK-409 103628-46-2, Sumatriptan 113563-71-6, (-)-Pinacidil 128270-60-0, Hirulog 129623-01-4, GR 82334 133052-90-1, GF 109203X 136553-81-6, BQ 123 138614-30-9, HOE 140 138680-92-9 142001-63-6, SR 48968 146535-11-7, AG 1296 149017-66-3, PPADS 159125-41-4 162626-99-5, FR 144420 188627-80-7, Integrelin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)

IT 64285-06-9, (+)-Anatoxin-A 92142-32-0 122564-82-3 **156223-05-1**, GTS-21 161416-43-9, A 84543 161416-98-4, A-85380 **161417-03-4**, **ABT-089 179120-52-6**, SIB-1765F **183288-99-5**, **RJR-2403 198283-73-7**, **ABT-594 203564-57-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)

IT **156223-05-1**, GTS-21 **161417-03-4**, **ABT-089 179120-52-6**, SIB-1765F **183288-99-5**, **RJR-2403 198283-73-7**, **ABT-594 203564-57-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)

RN 156223-05-1 HCAPLUS
CN 2,3'-Bipyridine, 3-[(2,4-dimethoxyphenyl)methylene]-3,4,5,6-tetrahydro-, dihydrochloride, (3E)- (9CI) (CA INDEX NAME)

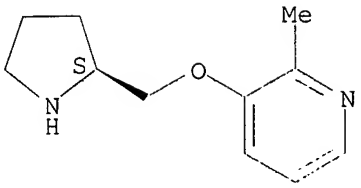
Double bond geometry as shown.



●2 HCl

RN 161417-03-4 HCAPLUS
CN Pyridine, 2-methyl-3-[(2S)-2-pyrrolidinylmethoxy]- (9CI) (CA INDEX NAME)

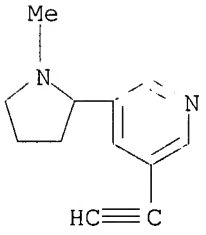
Absolute stereochemistry. Rotation (+).



RN 179120-52-6 HCAPLUS
CN Pyridine, 3-ethynyl-5-(1-methyl-2-pyrrolidinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

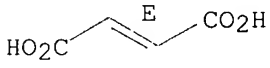
CRN 179120-51-5
CMF C12 H14 N2



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

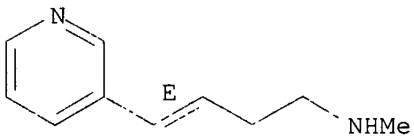


RN 183288-99-5 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



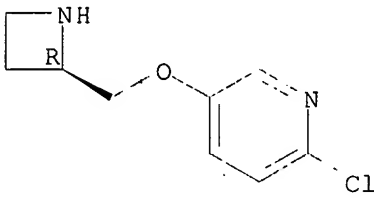
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

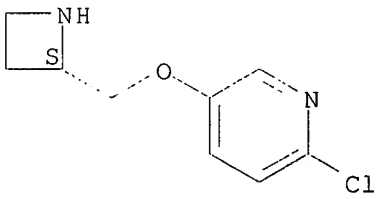
RN 198283-73-7 HCAPLUS
CN Pyridine, 5-[(2R)-2-azetidinylmethoxy]-2-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 203564-57-2 HCAPLUS
CN Pyridine, 5-[(2S)-2-azetidinylmethoxy]-2-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L130 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:116902 HCAPLUS
DN 132:161263
TI Pharmaceutical **composition** using a nicotinic compound and an acetylcholinesterase inhibitor for the prevention and treatment of central nervous system disorders
IN Bencherif, Merouane
PA R.J. Reynolds Tobacco Co., USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-645
ICS A61K031-645; A61K031-465
CC 1-11 (Pharmacology)
Section cross-reference(s): 27, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000007600	A1	20000217	WO 1999-US12243	19990602

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA,

ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6218383	B1	20010417	US 1998-130498	19980807	
CA 2335012	AA	20000217	CA 1999-2335012	19990602	
AU 9943285	A1	20000228	AU 1999-43285	19990602	
BR 9912805	A	20010502	BR 1999-12805	19990602	
EP 1102588	A1	20010530	EP 1999-965348	19990602	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002522390	T2	20020723	JP 2000-563285	19990602	
PRAI US 1998-130498	A	19980807			
WO 1999-US12243	W	19990602			

AB A pharmaceutical **compn.** incorporates a pharmaceutically effective amt. of at least two components, one of those components being a **nicotinic** compd. capable of interacting with **nicotinic cholinergic receptors** (e.g., a **nicotinic** agonist, such as E-**metanicotine**) and one of those components being an **acetylcholinesterase** inhibitor (e.g., tacrine). The pharmaceutical **compn.** is useful for treating CNS disorders, e.g. **Alzheimer**'s disease.

ST CNS therapeutic nicotinic compd acetylcholinesterase inhibitor; **Alzheimer** drug nicotinic compd acetylcholinesterase inhibitor; **metanicotine** tacrine CNS therapeutic **Alzheimer** drug

IT Amines, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(arom.; nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

IT **Cognition enhancers**
Drug delivery systems
Drug interactions
Nervous system agents
Nicotinic agonists
(nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

IT **Nicotinic receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**nicotinic** compd. and **acetylcholinesterase** inhibitor for prevention and treatment of central nervous system disorders)

IT 9000-81-1, Acetylcholinesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

IT 252870-54-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

IT 321-64-2, Tacrine **15585-43-0, E-Metanicotine**
252870-53-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

IT 252870-91-0P 252870-93-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction; nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

IT 74-89-5, Methylamine, reactions 98-59-9, p-Toluenesulfonyl chloride 526-99-8, Galactaric acid 64584-92-5, (2R)-4-Penten-2-ol 212332-40-6, 5-Bromo-3-isopropoxypyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

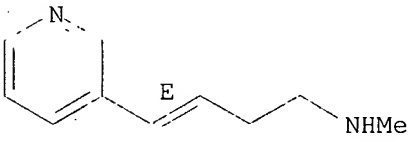
RE

(1) Andrulis, P; US 5434170 A 1995 HCAPLUS
(2) Dull, G; US 5597919 A 1997 HCAPLUS
(3) Madhukar, D; US 5726316 A 1998 HCAPLUS
(4) Nikolov, R; DRUG NEWS AND PERSPECTIVES 1998, V11/4, P248
(5) Sibia Neurosciences Inc; WO 9631475 A 1996 HCAPLUS
(6) Woolf, T; US 5466696 A 1995 HCAPLUS

IT **15585-43-0**, E-**Metanicotine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nicotinic compd. and acetylcholinesterase inhibitor for prevention and treatment of central nervous system disorders)

RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

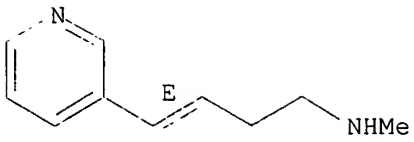


L130 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:565910 HCAPLUS
DN 131:194296
TI Method using a **metanicotine**-based compound for the treatment of pain, including chronic and female-specific pain
IN Eisenach, James C.
PA Wake Forest University, USA
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-44
CC 1-11 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9943322	A1	19990902	WO 1999-US3896	19990224
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321991	AA	19990902	CA 1999-2321991	19990224

AU 9933080 A1 19990915 AU 1999-33080 19990224
BR 9908190 A 20001024 BR 1999-8190 19990224
EP 1056458 A1 20001206 EP 1999-936030 19990224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002504512 T2 20020212 JP 2000-533119 19990224
US 6248744 B1 20010619 US 2000-622675 20001005
PRAI US 1998-75794P P 19980224
WO 1999-US3896 W 19990224
OS MARPAT 131:194296
AB Patients susceptible to, or suffering from chronic and/or female-specific pain are treated by administering an effective amt. of a **metanicotine**-based compd.
ST **metanicotine** deriv analgesic chronic female pain
IT Pain
(chronic; **metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
IT Bone, disease
(degeneration, pain resulting from; **metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
IT Disease, animal
(degenerative, bone, pain resulting from; **metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
IT Analgesics
Sex
(**metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
IT Arthritis
Injury
Menstruation
Neoplasm
Ovulation
Parturition
Pregnancy
(pain resulting from; **metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
IT **15585-43-0**, trans-**Metanicotine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bencherif; US 5811442 A 1998 HCAPLUS
(2) Caldwell; US 5212188 A 1993 HCAPLUS
(3) Caldwell; US 5861423 A 1999 HCAPLUS
(4) Dull; US 5616716 A 1997 HCAPLUS
(5) Smith; US 5604231 A 1997 HCAPLUS
(6) Teng; US 5663357 A 1997 HCAPLUS
IT **15585-43-0**, trans-**Metanicotine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**metanicotine**-based compd. for treatment of pain, including chronic and female-specific pain)
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



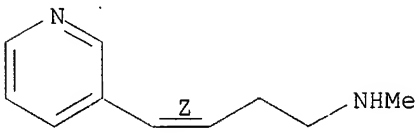
L130 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:130573 HCAPLUS
DN 130:177543
TI Aryl-substituted olefinic amines and pharmaceutical compositions thereof for eliciting analgesic effects
IN Martin, Billy R.; Damaj, Mohamad L.
PA Virginia Commonwealth University, USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A61K031-44
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9907369	A1	19990218	WO 1998-US16485	19980807
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 5914337	A	19990622	US 1997-908440	19970807
	AU 9889004	A1	19990301	AU 1998-89004	19980807
	EP 1011672	A1	20000628	EP 1998-940814	19980807
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6117891	A	20000912	US 1999-257368	19990225
PRAI	US 1997-908440	A	19970807		
	WO 1998-US16485	W	19980807		

OS MARPAT 130:177543
AB The invention relates to treatment of pain with a new class of analgesic compds. More particularly, the invention relates to a method for reducing pain of a patient involving administering to a patient an effective amt. of an aryl-substituted olefinic amine compd. In one aspect, the inventive method of reducing pain in a patient involves use of **metanicotine** compds. as the analgesic agent.
ST aryl olefinic amine analgesic; **metanicotine** compd analgesic
IT Analgesics
(aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
IT Drug delivery systems
(injections, i.m.; aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
IT Drug delivery systems
(injections, i.v.; aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
IT Drug delivery systems
(injections, intracerebroventricular; aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)

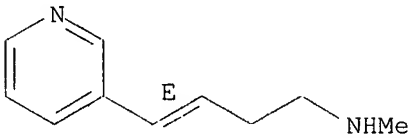
IT Drug delivery systems
(injections, intrathecal; aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
IT Drug delivery systems
(injections, s.c.; aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
IT **1129-68-6D**, derivs. **15585-43-0D**, derivs. 180740-75-4
220662-90-8 220662-91-9 220662-92-0 220662-93-1D, derivs.
220662-94-2D, derivs. **220662-95-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Watson; J Ethnopharmacol 1983, V8(3), P303 HCAPLUS
IT **1129-68-6D**, derivs. **15585-43-0D**, derivs.
220662-95-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl-substituted olefinic amines and pharmaceutical compns. thereof for analgesics)
RN 1129-68-6 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

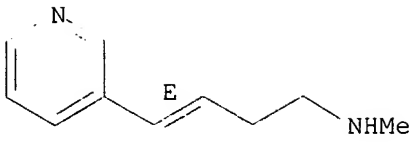


RN 220662-95-3 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

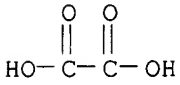
CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



CM 2

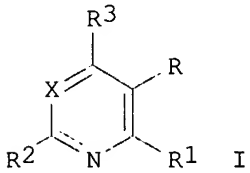
CRN 144-62-7
CMF C2 H2 O4



L130 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:618370 HCAPLUS
DN 129:260345
TI Preparation of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists
IN Bencherif, Merouane; Lippiello, Patrick Michael
PA USA
SO U.S., 15 pp.
CODEN: USXXAM
DT **Patent**
LA English
IC ICM A01N043-64
ICS A61K031-44
NCL 514384000
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5811442	A	19980922	US 1997-804224	19970221
PRAI	US 1997-804224		19970221		

OS MARPAT 129:260345
GI



I

AB Title compds. [I; R = CR4:CR5[C(R6)2]nNR7R8; R1-R3 = H, halo, alkyl, (di)(alkyl)amino; R4-R6 = H or (halo)alkyl; R7 = H or alkyl; R8 = H, (cyclo)alkyl, (hetero)aryl, etc.; NR7R8 = heterocyclyl; X = N or CR9; R9 = Halo, OH, cyano, acyl, etc.; n = 1-8] were prepd. Thus, 3,5-dibromopyridine was arylated by PhB(OH)2 and the product alkenylated by MeCH:CHCH2OH to give, after amination, (E)-PhZCMe:CHCH2NHMe (Z = 5,3-pyridinediyl). Data for biol. activity of I were given.
ST pyridylbutenamine prepn **nicotinic receptor** agonist;

vasodilator pyridylbutenamine prepn

IT Blood vessel, disease
(Raynaud's phenomenon, treatment; prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

IT Circulation
(microcirculation; prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

IT Vasodilators
(prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

IT **Nicotinic receptors**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

IT **1129-68-6P**, (Z)-**Metanicotine** **15585-43-0P**, (E)-**Metanicotine** 212332-28-0P 212332-29-1P 212332-30-4P 212332-31-5P 212332-32-6P 212332-33-7P 212332-35-9P 212332-36-0P 212332-44-0P 213386-90-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

IT 67-63-0, 2-Propanol, reactions 98-80-6, Phenylboronic acid 100-51-6, Benzenemethanol, reactions 139-02-6, Sodium phenoxide 625-92-3, 3,5-Dibromopyridine 627-27-0, 3-Buten-1-ol 20826-04-4, 5-Bromonicotinic acid 52898-32-5, N-(3-Butenyl)phthalimide 189274-78-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

IT 28232-63-5P, 3-Bromo-5-phenoxypyridine 37669-64-0P, 3-Bromo-5-hydroxymethylpyridine 130722-95-1P, 3-Bromo-5-benzyloxypyridine 142137-17-5P, 3-Bromo-5-phenylpyridine 173999-17-2P, 3-Bromo-5-methoxymethylpyridine 212332-37-1P 212332-38-2P 212332-39-3P 212332-40-6P, 3-Bromo-5-isopropoxypyridine 212332-41-7P 212332-42-8P 212332-43-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)

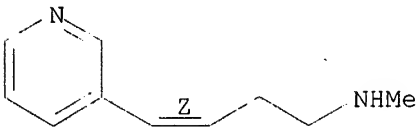
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Acheson; J Chem Soc, Perkins Trans, 1 1980, P579 HCAPLUS
(2) Anon; WO 9620600 1996 HCAPLUS
(3) Bencherif; J of Pharmacology and Exper Therapeutics 1996, V279(3), P1413 HCAPLUS
(4) Bencherif; J of Pharmacology and Exper Therapeutics 1996, V279(3), P1413 HCAPLUS
(5) Caldwell; US 5212188 1993 HCAPLUS
(6) Cosford; US 5585388 1996 HCAPLUS
(7) Crooks; US 5616707 1997 HCAPLUS
(8) Dull; US 5597919 1997 HCAPLUS
(9) Dull; US 5616716 1997 HCAPLUS
(10) Henrich; Kim Wochenschr 1984, V62(Suppl II), P92
(11) Jinno; Nicotine and acetylcholine induce release of calcitonin gene-related peptide from rat trachea 1994, P1651 HCAPLUS
(12) Laforge; J Amer Chem Soc 1928, V50, P2477 HCAPLUS
(13) Lippiello; J of Pharmacology and Exper Therapeutics 1996, V279(3), P1422 HCAPLUS
(14) Smith; US 5604231 1997 HCAPLUS
(15) Wilson; J of Pharmacology and Exper Therapeutics 1976, V196(3), P685

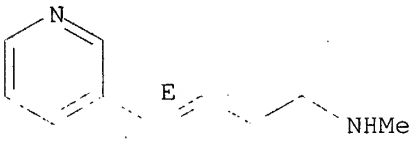
HCAPLUS
IT **1129-68-6P, (Z)-Metanicotine 15585-43-0P, (E)-Metanicotine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(3-pyridyl)-3-buten-1-amines and analogs as vasodilating **nicotinic receptor** agonists)
RN 1129-68-6 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

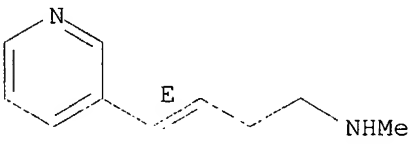


L130 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:597499 HCAPLUS
DN 127:262606
TI Preparation of .omega.-arylalkenamines as nervous system agents
IN Ruecroft, Graham; Woods, Martin
PA UK
SO U.S., 5 pp.
CODEN: USXXAM
DT **Patent**
LA English
IC ICM C07D213-62
NCL 546300000
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5663356	A	19970902	US 1996-635165	19960423
	WO 9740013	A1	19971030	WO 1997-US6573	19970422
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9727360	A1	19971112	AU 1997-27360	19970422
PRAI	US 1996-635165		19960423		
	WO 1997-US6573		19970422		

OS CASREACT 127:262606; MARPAT 127:262606
AB (E)-RCH:CH(CH2)nNHMe (R = aryl, n = 1-4) were prepd. as nervous system agents (no data). Thus, **nicotine** was converted to (E)-**metanicotine** in 3 steps.
ST arylalkenamine prepn nervous system agent
IT Nervous system agents
(.omega.-arylalkenamines)
IT **15585-43-0P**, 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (E)-
183288-99-5P 196399-54-9P, 5-Bromometanicotine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .omega.-arylalkenamines as nervous system agents)
IT **54-11-5, Nicotine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of .omega.-arylalkenamines as nervous system agents)
IT **196399-55-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .omega.-arylalkenamines as nervous system agents)
IT **15585-43-0P**, 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (E)-
183288-99-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of .omega.-arylalkenamines as nervous system agents)
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

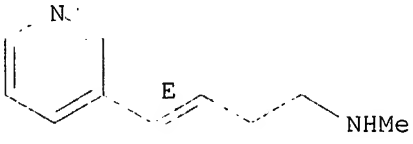


RN 183288-99-5 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



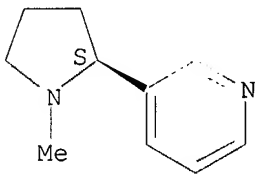
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

IT **54-11-5, Nicotine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of .omega.-arylalkenamines as nervous system agents)
RN 54-11-5 HCAPLUS
CN Pyridine, 3-[(2S)-1-methyl-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

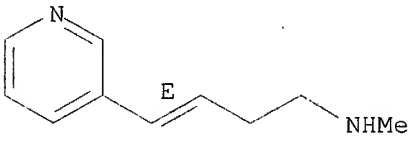


IT **196399-55-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .omega.-arylalkenamines as nervous system agents)
RN 196399-55-0 HCAPLUS
CN Carbamic acid, ethyl-, compd. with (E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (1:1) (9CI) (CA INDEX NAME)

CM 1

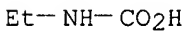
CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



CM 2

CRN 7409-13-4
CMF C3 H7 N O2



L130 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:551340 HCAPLUS
DN 125:185891
TI Pharmaceutical **compositions** with aryl-substituted compounds, and their preparation, for prevention and treatment of ulcerative colitis
IN Smith, Carr Joseph; Lippiello, Patrick Michael; Bencherif, Merouane; Caldwell, William Scott; Dull, Gary Maurice
PA R.J. Reynolds Tobacco Company, USA
SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A01N043-40
ICS A01N043-54; A61K031-435; A61K031-44; A61K031-505
CC 1-9 (Pharmacology)
Section cross-reference(s): 27, 28
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9620599	A1	19960711	WO 1995-US16901	19951227
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5604231	A	19970218	US 1995-364980	19950106
AU 9645295	A1	19960724	AU 1996-45295	19951227
EP 873050	A1	19981028	EP 1995-943979	19951227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10512857	T2	19981208	JP 1995-521129	19951227
PRAI US 1995-364980		19950106		
WO 1995-US16901		19951227		

OS MARPAT 125:185891
AB Patients suffering from or susceptible to an idiopathic chronic inflammatory bowel disease (e.g., ulcerative colitis) are treated with pharmaceutical **compns**. Those patients are treated by administration of an effective amt. of aryl-substituted aliph. compd., an aryl-substituted olefinic amine compd. or an aryl-substituted acetylenic compd. Exemplary compds. are (E)-4-(5-pyrimidinyl)-3-butene-1-amine, (E)-4-[3-(5-methoxypyridin)yl]-3-butene-1-amine, (E)-N-methyl-4-(5-pyrimidinyl)-3-butene-1-amine, (E)-N-methyl-4-[3-(5-methoxypyridin)yl]-3-butene-1-amine, (E)-**metanicotine**, (Z)-**metanicotine**, N-methyl-(3-pyridinyl)-butane-1-amine, N-methyl-4-(3-pyridinyl)-3-butyne-1-amine and (E)-N-methyl-4-[3-(6-methylpyridin)yl]-3-butene-1-amine. Prepn. of compds. of the invention is described. Compds. of the invention were tested for e.g. **nicotinic receptor** binding.
ST aryl compd prepn ulcerative colitis
IT Intestine, disease
(inflammatory, aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT **Receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**nicotinic**, aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT Intestine, disease
(ulcerative colitis, aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT **1129-68-6P** 3000-74-6P **15585-43-0P** 180740-72-1P
180740-75-4P 180740-78-7P 180740-82-3P 180915-52-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT 180740-83-4P 180740-84-5P 180740-85-6P **180915-55-3P**
180915-56-4P 180915-57-5P 180915-58-6P 180915-60-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT 180740-71-0P 180740-77-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 180915-53-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 63671-82-9P 77629-49-3P 90872-72-3P 101540-79-8P 138487-20-4P 180740-70-9P 180740-73-2P 180740-74-3P 180740-76-5P 180740-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; aryl-substituted compd. prepn. for treatment of ulcerative colitis)

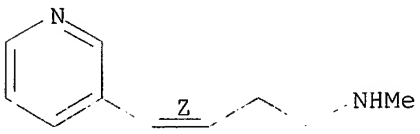
IT 88-12-0, reactions 109-72-8, n-Butyl lithium, reactions 110-17-8, Fumaric acid, reactions 500-22-1, Pyridine-3-carboxaldehyde 541-41-3, Ethyl chloroformate 558-13-4, Tetrabromomethane 4595-59-9, 5-Bromopyrimidine 21684-59-3, Ethyl 6-methylnicotinate 24424-99-5, Di-tert-butyl dicarbonate 50720-12-2, 3-Bromo-5-methoxypyridine 52898-32-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 51-61-6, Dopamine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(release; aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT **1129-68-6P 15585-43-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

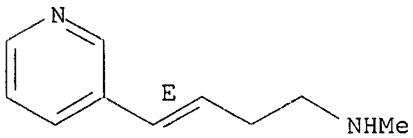
RN 1129-68-6 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



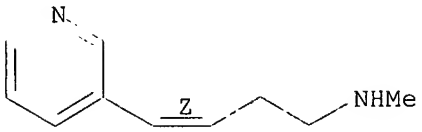
IT **180915-55-3P 180915-56-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

RN 180915-55-3 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 1129-68-6
CMF C10 H14 N2

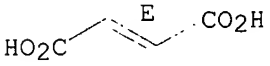
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

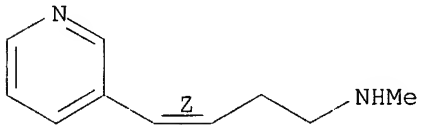


RN 180915-56-4 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 1129-68-6
CMF C10 H14 N2

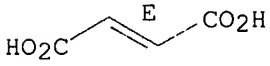
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



L130 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:551339 HCAPLUS
DN 125:185904
TI Pharmaceutical **compositions** with aryl-substituted compounds, and their preparation, for prevention and treatment of central nervous system disorders

IN Bencherif, Merouane; Lippiello, Patrick Michael; Caldwell, William Scott; Dull, Gary Maurice
PA R.J. Reynolds Tobacco Company, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM A01N043-40
ICS A01N043-54; A61K031-44; A61K031-505
CC 1-11 (Pharmacology)
Section cross-reference(s): 27, 28
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9620600	A1	19960711	WO 1995-US17034	19951228
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5597919	A	19970128	US 1995-364979	19950106
	US 5731314	A	19980324	US 1995-364978	19950106
	US 5824692	A	19981020	US 1995-364977	19950106
	AU 9646108	A1	19960724	AU 1996-46108	19951228
	EP 801527	A1	19971022	EP 1995-944268	19951228
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 2001520628	T2	20011030	JP 1996-521171	19951228
	US 5885998	A	19990323	US 1998-23040	19980212
	US 6107298	A	20000822	US 1999-267553	19990312
PRAI	US 1995-364977	A1	19950106		
	US 1995-364978	A1	19950106		
	US 1995-364979	A1	19950106		
	WO 1995-US17034	W	19951228		
	US 1998-23040	A3	19980212		

OS MARPAT 125:185904
AB Patients susceptible to or suffering from central nervous system disorders (e.g., **Tourette**'s syndrome, attention deficit disorder, or **schizophrenia**) are treated by administering an effective amt. of an aryl-substituted aliph. compd., an aryl-substituted olefinic amine compd., or an aryl-substituted acetylenic compd. Exemplary compds. are (E)-4-(5-pyrimidinyl)-3-butene-1-amine, (E)-4-[3-(5-methoxypyridin)yl]-3-butene-1-amine, (E)-N-methyl-4-(5-pyrimidinyl)-3-butene-1-amine, (E)-N-methyl-4-[3-(5-methoxypyridin)yl]-3-butene-1-amine, (Z)-**metanicotine**, (E)-**metanicotine**, N-methyl-(3-pyridinyl)-butane-1-amine, N-methyl-4-(3-pyridinyl)-3-butyne-1-amine and (E)-N-methyl-4-[3-(6-methylpyridin)yl]-3-butene-1-amine. Prepn. of compds. of the invention is described. Compds. of the invention were tested for e.g. **nicotinic receptor** binding.
ST central nervous system disorder aryl compd; aryl compd prepn CNS disorder
IT Nervous system agents
Parkinsonism
Schizophrenia
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT **Mental disorder**
(**Alzheimer**'s disease, aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT **Mental disorder**
(**Alzheimer**'s disease, type I, aryl-substituted compd. prepn. for treatment of ulcerative colitis)
IT Brain, disease
(Gilles de la **Tourette**, aryl-substituted compd. prepn. for

treatment of ulcerative colitis)

IT **Mental disorder**
(**attention deficit**, aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT **Nervous system**
(central, **disease**, aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT **Receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**nicotinic**, aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT **1129-68-6P** 3000-74-6P **15585-43-0P** 180740-72-1P
180740-75-4P 180740-78-7P 180740-82-3P 180915-52-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 180740-83-4P 180740-84-5P 180740-85-6P 180915-54-2P
180915-55-3P 180915-56-4P 180915-57-5P 180915-58-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 180740-71-0P 180740-77-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 180915-53-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 13270-46-7P 63671-82-9P 77629-49-3P 90872-72-3P 138487-20-4P
180740-70-9P 180740-73-2P 180740-74-3P 180740-76-5P 180740-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; aryl-substituted compd. prepn. for treatment of ulcerative colitis)

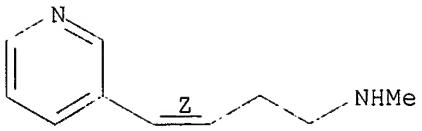
IT 88-12-0, reactions 109-72-8, n-Butyl lithium, reactions 110-17-8, Fumaric acid, reactions 500-22-1, Pyridine-3-carboxaldehyde 541-41-3, Ethyl chloroformate 558-13-4, Tetrabromomethane 4595-59-9, 5-Bromopyrimidine 21684-59-3, Ethyl 6-methylnicotinate 24424-99-5, Di-tert-butyl dicarbonate 50720-12-2, 3-Bromo-5-methoxypyridine 52898-32-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT 51-61-6, Dopamine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(release; aryl-substituted compd. prepn. for treatment of ulcerative colitis)

IT **1129-68-6P 15585-43-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)

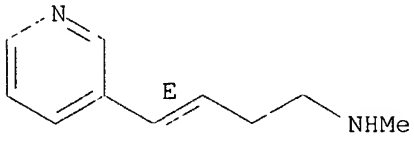
RN 1129-68-6 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

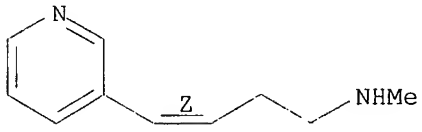


IT **180915-55-3P 180915-56-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(aryl-substituted compd. prepn. for treatment of ulcerative colitis)
RN 180915-55-3 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 1129-68-6
CMF C10 H14 N2

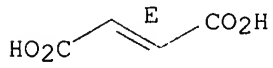
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

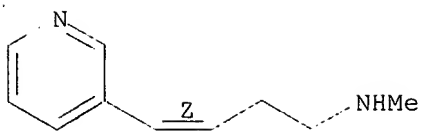


RN 180915-56-4 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 1129-68-6
CMF C10 H14 N2

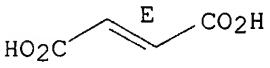
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



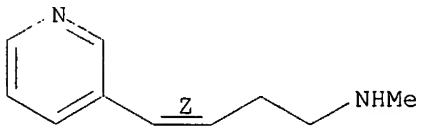
L130 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1996:544083 HCAPLUS
DN 125:185907
TI Pharmaceutical **compositions** for prevention and treatment of central nervous system disorders
IN Crooks, Peter Anthony; Caldwell, William Scott; Dull, Gary Maurice; Bhatti, Baldwinder Singh
PA R.J. Reynolds Tobacco Company, USA; University of Kentucky Research Foundation
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT **Patent**
LA English
IC ICM C07D213-02
ICS C07D239-24
CC 1-11 (Pharmacology)
Section cross-reference(s): 27
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9620929	A1	19960711	WO 1995-US16903	19951227
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5616707	A	19970401	US 1995-364976	19950106
	AU 9646455	A1	19960724	AU 1996-46455	19951227
	EP 801646	A1	19971022	EP 1995-944395	19951227
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 11501294	T2	19990202	JP 1995-521130	19951227
	US 5726316	A	19980310	US 1997-784615	19970121
PRAI	US 1995-364976		19950106		
	WO 1995-US16903		19951227		

OS MARPAT 125:185907
AB Patients susceptible to or suffering from central nervous system disorders are treated by administering an effective amt. of an aryl substituted olefinic amine compd. or an aryl substituted acetylenic compd. Exemplary compds. are (E)-N-methyl-4-[3-(6-methylpyridin)yl]-3-butane-1-amine and N-methyl-4-(3-pyridinyl)-3-butyne-1-amine.

ST amine central nervous system disorder
IT Amines, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(alkenyl, aryl and olefinic amines for prevention and treatment of central nervous system disorders)
IT Amines, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl, aryl and olefinic amines for prevention and treatment of central nervous system disorders)
IT **Nervous system**
(central, **disease**, aryl and olefinic amines for prevention and treatment of central nervous system **disorders**)
IT **1129-68-6P**, (Z)-**Metanicotine** 3000-74-6P
15585-43-0P, (E)-**Metanicotine** 180740-71-0P
180740-72-1P 180740-75-4P 180740-77-6P 180740-78-7P
180740-80-1P 180740-82-3P 180740-83-4P 180740-84-5P
180740-85-6P 180915-52-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl and olefinic amines for prevention and treatment of central nervous system disorders)
IT 50-00-0, Formaldehyde, reactions 74-89-5, Methylamine, reactions 88-12-0, reactions 110-17-8, Fumaric acid, reactions 124-63-0, Methane sulfonyl chloride 302-01-2, Hydrazine, reactions 500-22-1, Pyridine 3-carboxaldehyde 558-13-4, Tetrabromomethane 4595-59-9, 5-Bromopyrimidine 21684-59-3, Ethyl 6-methylnicotinate 24424-99-5, Di-tert-butyl dicarbonate 50720-12-2, 3-Bromo-5-methoxypyridine 52898-32-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(aryl and olefinic amines for prevention and treatment of central nervous system disorders)
IT 13270-56-9P, 6-Methylnicotine 63671-82-9P 77629-49-3P, 6-Methylmyosmine 90872-72-3P 138487-20-4P 180740-70-9P 180740-73-2P 180740-74-3P 180740-76-5P 180740-79-8P 180740-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(aryl and olefinic amines for prevention and treatment of central nervous system disorders)
IT **1129-68-6P**, (Z)-**Metanicotine** **15585-43-0P**, (E)-**Metanicotine** **180740-80-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl and olefinic amines for prevention and treatment of central nervous system disorders)
RN 1129-68-6 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI) (CA INDEX NAME)

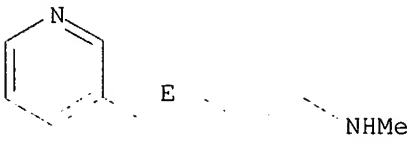
Double bond geometry as shown.



RN 15585-43-0 HCAPLUS

CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

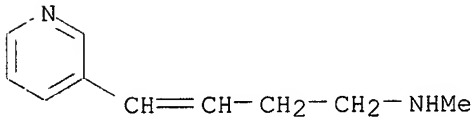
Double bond geometry as shown.



RN 180740-80-1 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

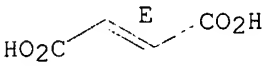
CRN 538-79-4
CMF C10 H14 N2



CM 2

CRN 110-17-8
CMF C4 H4 O4

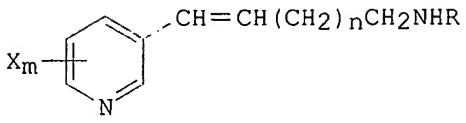
Double bond geometry as shown.



L130 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:486060 HCAPLUS
DN 119:86060
TI Method for treatment of neurodegenerative diseases
IN Caldwell, William S.; Lippiello, Patrick M.
PA Reynolds, R. J., Tobacco Co., USA
SO U.S., 5 pp.
CODEN: USXXAM
DT **Patent**
LA English
IC A61U031-44
NCL 514343000
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5212188	A	19930518	US 1992-844364	19920302
	EP 559413	A1	19930908	EP 1993-301534	19930301
	EP 559413	B1	19960925		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 06024983	A2	19940201	JP 1993-62489	19930301
	AT 143263	E	19961015	AT 1993-301534	19930301

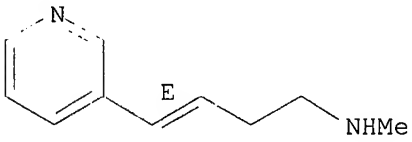
ES 2093361 T3 19961216 ES 1993-301534 19930301
PRAI US 1992-844364 19920302
OS MARPAT 119:86060
GI



I

AB Disclosed is the method for treating a patient suffering from senile dementia of the **Alzheimer**'s type, the method **comprising** administering to the patient an effective amt. of a compd. having the **formula** I where n = integer 1-5, m = 0 - 4, R = H or alkyl, and X = alkyl or halo. Trans-meta-**nicotine** has the capability of passing the blood-brain barrier, binding to high affinity **nicotinic receptors**, and eliciting neurotransmitter secretion. Apparently, I have the capability of being useful in treating neurodegenerative diseases.
ST **nicotine** deriv pharmacol brain disease
IT Nerve, disease
(treatment of degenerative, with **nicotine** derivs.)
IT **Mental disorder**
(**Alzheimer**'s disease, treatment of, with **nicotine** derivs.)
IT **15585-43-0D**, trans-Meta-**nicotine**, derivs.
RL: BIOL (Biological study)
(neurodegenerative disease treatment by)
IT **15585-43-0D**, trans-Meta-**nicotine**, derivs.
RL: BIOL (Biological study)
(neurodegenerative disease treatment by)
RN 15585-43-0 HCAPLUS
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



=> fil embase
FILE 'EMBASE' ENTERED AT 10:59:43 ON 04 MAR 2003

FILE COVERS 1974 TO 27 Feb 2003 (20030227/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l161

L161 ANSWER 1 OF 4 EMBASE
AN 2003017547 EMBASE

TI Modulation of inhibitory synaptic activity by a non-.alpha.4.beta.2, non-.alpha.7 subtype of nicotinic receptors in the substantia gelatinosa of adult rat spinal cord.

AU Takeda D.; Nakatsuka T.; Papke R.; Gu J.G.
CS J.G. Gu, Department of Oral Surgery, College of Dentistry, University of Florida, 1600 SW Archer Road, Gainesville, FL 32610, United States. jgu@dental.ufl.edu

SO Pain, (2003) 101/1-2 (13-23).
Refs: 60
ISSN: 0304-3959 CODEN: PAINDB
CY Netherlands
DT Journal; Article
FS 008 Neurology and Neurosurgery
029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English

AB The GABA/glycine-mediated inhibitory activity in the substantia gelatinosa (SG) of the spinal cord is critical in the control of nociceptive transmission. We examined whether and how SG inhibitory activity might be regulated by neuronal nicotinic receptors (nAChRs). Patch-clamp recordings were performed in SG neurons of spinal slice preparations from adult rats. We provided electrophysiological evidence that inhibitory presynaptic terminals in the SG expressed nAChRs and their activation resulted in large increases in the frequency of spontaneous and miniature inhibitory postsynaptic currents (sIPSCs and mIPSCs) in over 90% SG neurons tested. The enhancement of inhibitory activity was mediated by increases in the release of GABA/glycine, and direct Ca(2+) entry through SG presynaptic nAChRs appeared to be involved. Miniature IPSC frequency could be enhanced by the nAChR agonists **nicotine** or cytisine. **Nicotine** could still elicit large increases in mIPSC frequency in the presence of the .alpha.4.beta.2 nAChR antagonist dihydro-beta-erythroidine (5.mu.M) and the .alpha.7 nAChR-selective antagonist methyllycaconitine (40nM). However, **nicotine** did not produce a significant enhancement of mIPSC frequency in the presence of the broad spectrum nAChR antagonist **mecamylamine** (5.mu.M). Nicotinic agonist-evoked whole-cell currents from SG neurons and the antagonist profiles also indicated the presence of a subtype of nAChRs, which were different from the major central nervous system nAChR subtypes, i.e. .alpha.4.beta.2* or .alpha.7 nAChRs. Together, our results suggest that a subtype of nAChR, possibly .alpha.3.beta.4* nAChR or a new nAChR type, is highly expressed at the inhibitory presynaptic terminals in SG of adult rats and play a role in the control of inhibitory activity in SG. .COPYRGT. 2002 International Association for the Study of Pain. Published by Elsevier Science B.V. All rights reserved.

CT Medical Descriptors:
***synapse**
***substantia gelatinosa**
***spinal cord**
patch clamp
electrophysiology
nerve ending
protein expression
inhibitory postsynaptic potential
4 aminobutyric acid release
protein secretion
calcium transport
drug effect
drug selectivity
protein localization
nonhuman
rat
controlled study

animal tissue
article
priority journal
Drug Descriptors:
***nicotinic receptor: EC, endogenous compound**
*receptor subtype: EC, endogenous compound
4 aminobutyric acid: EC, endogenous compound
glycine: EC, endogenous compound
calcium ion: EC, endogenous compound
nicotinic agent: CB, drug combination
nicotinic agent: PD, pharmacology
cytisine: PD, pharmacology
nicotine: CB, drug combination
nicotine: PD, pharmacology
nicotinic receptor blocking agent: CB, drug combination
nicotinic receptor blocking agent: PD, pharmacology
dihydro beta erythroidine: CB, drug combination
dihydro beta erythroidine: PD, pharmacology
methyllycaconitine: CB, drug combination
methyllycaconitine: PD, pharmacology
mecamylamine: CB, drug combination
mecamylamine: PD, pharmacology
6 cyano 7 nitro 2,3 quinoxalinedione: CB, drug combination
6 cyano 7 nitro 2,3 quinoxalinedione: PD, pharmacology
2 amino 5 phosphonovaleric acid: CB, drug combination
2 amino 5 phosphonovaleric acid: PD, pharmacology
strychnine: PD, pharmacology
bicuculline: PD, pharmacology
n methyl 4 (3 pyridinyl) 3 butenamine: PD, pharmacology
choline: PD, pharmacology
RN (4 aminobutyric acid) 28805-76-7, 56-12-2; (glycine) 56-40-6, 6000-43-7, 6000-44-8; (calcium ion) 14127-61-8; (cytisine) 485-35-8; (**nicotine**) **54-11-5**; (dihydro beta erythroidine) 23255-54-1; (methyllycaconitine) 21019-30-7, 72629-98-2; (**mecamylamine**) **60-40-2, 826-39-1**; (6 cyano 7 nitro 2,3 quinoxalinedione) 115066-14-3; (2 amino 5 phosphonovaleric acid) 76726-92-6; (strychnine) 1421-86-9, 57-24-9; (bicuculline) 485-49-4; (n methyl 4 (3 pyridinyl) 3 butenamine) **183288-99-5**; (choline) 123-41-1, 13232-47-8, 1927-06-6, 4858-96-2, 62-49-7, 67-48-1
CN **(1) Rjr 2403**
CO (1) Tocris (United States); RBI (United States); Sigma (United States)

L161 ANSWER 2 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001082029 EMBASE
TI Nicotinic treatment of Alzheimer's disease.
AU Newhouse P.A.; Potter A.; Kelton M.; Corwin J.
CS Dr. P.A. Newhouse, Univ. of Vermont College of Medicine, University Health Center, Department of Psychiatry, 1 South Prospect Street, Burlington, VT 05401-1195, United States
SO Biological Psychiatry, (1 Feb 2001) 49/3 (268-278).
Refs: 67
ISSN: 0006-3223 CODEN: BIPCBF
PUI S 0006-3223(00)01069-6
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Approximately 20 years after the formulation of the "cholinergic

hypothesis" to explain the cognitive symptoms of Alzheimer's disease, cholinesterase therapy remains the mainstay of treatment for this disorder. Although partially effective, currently available agents have limited effects on cognitive function and long-term efficacy appears modest. Direct or indirect stimulation of nicotinic cholinergic receptors may offer an additional therapeutic strategy. Ongoing investigations of the molecular substructure of central nervous system nicotinic receptors, their accompanying pharmacology, and the effects of nicotinic agents on cognitive function have suggested the possibility that nicotinic stimulation may have beneficial effects in Alzheimer's disease and other neuropsychiatric disorders. Studies from our laboratory and others have explored the role of central nervous system nicotinic mechanisms in normal human cognitive and behavioral functioning as well as their role in Alzheimer's disease. Results from acute therapeutic trials with **nicotine** and novel nicotinic agents suggest that nicotinic stimulation in Alzheimer's disease patients can improve the acquisition and retention of verbal and visual information and decrease errors in cognitive tasks, as well as improve accuracy and response time. Whether such results will translate into improved clinical functioning remains to be fully tested. Development of subtype-selective nicotinic agonists with an improved safety profile will enable long-term testing of the efficacy of nicotinic stimulation on cognitive performance as well as potential cytoprotective effects. Direct or indirect (allosteric) modulation of nicotinic receptor function offers a new opportunity for Alzheimer's disease therapeutics. .COPYRGT. 2001 Society of Biological Psychiatry.

CT Medical Descriptors:
***Alzheimer disease: DT, drug therapy**
cognition
hypothesis
treatment outcome
long term exposure
stimulation
central nervous system
chemical structure
drug mechanism
neuropsychiatry
visual information
verbal behavior
response time
clinical feature
drug efficacy
allosterism
dose response
vomiting: SI, side effect
anxiety
nausea: SI, side effect
cholinesterase inhibition
human
nonhuman
clinical trial
article
priority journal
Drug Descriptors:
***nicotine: AE, adverse drug reaction**
***nicotine: CT, clinical trial**
***nicotine: DO, drug dose**
***nicotine: DT, drug therapy**
***nicotine: IV, intravenous drug administration**
***nicotine: SC, subcutaneous drug administration**
***nicotine: TD, transdermal drug administration**
*nicotinic receptor blocking agent: CT, clinical trial
***nicotinic receptor blocking agent: CB, drug combination**
*nicotinic receptor blocking agent: CM, drug comparison

*nicotinic receptor blocking agent: DT, drug therapy
*nicotinic receptor blocking agent: PD, pharmacology
***mecamylamine: CT, clinical trial**
***mecamylamine: CM, drug comparison**
***mecamylamine: DO, drug dose**
***mecamylamine: DT, drug therapy**
***mecamylamine: PD, pharmacology**
***mecamylamine: PO, oral drug administration**
muscarinic receptor blocking agent: CB, drug combination
muscarinic receptor blocking agent: CM, drug comparison
muscarinic receptor blocking agent: PD, pharmacology
cholinesterase: DT, drug therapy
scopolamine: CB, drug combination
scopolamine: CM, drug comparison
scopolamine: PD, pharmacology
atropine: CB, drug combination
atropine: CM, drug comparison
atropine: PD, pharmacology
3 methyl 5 (1 methyl 2 pyrrolidinyl)isoxazole: AE, adverse drug reaction
3 methyl 5 (1 methyl 2 pyrrolidinyl)isoxazole: CT, clinical trial
3 methyl 5 (1 methyl 2 pyrrolidinyl)isoxazole: DT, drug therapy
3 methyl 5 (1 methyl 2 pyrrolidinyl)isoxazole: PD, pharmacology
3 (2,4 dimethoxybenzylidene)anabaseine: DT, drug therapy
3 (2,4 dimethoxybenzylidene)anabaseine: PD, pharmacology
4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol: DT, drug therapy
4 [[2 (1 methyl 2 pyrrolidinyl)ethyl]thio]phenol: PD, pharmacology
n methyl 4 (3 pyridinyl) 3 butenamine: DT, drug therapy
n methyl 4 (3 pyridinyl) 3 butenamine: PD, pharmacology
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine: AE, adverse drug reaction
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine: CT, clinical trial
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine: DT, drug therapy
3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine: PD, pharmacology
nicotinic agent: CM, drug comparison
nicotinic agent: PD, pharmacology

RN (**nicotine**) **54-11-5**; (**mecamylamine**) **60-40-2, 826-39-1**; (cholinesterase) 9001-08-5; (scopolamine) 138-12-5, 51-34-3, 55-16-3; (atropine) 51-55-8, 55-48-1; (**3 methyl** 5 (**1 methyl 2 pyrrolidinyl**)**isoxazole**) **147402-53-7**; (**3** (**2,4 dimethoxybenzylidene**) **anabaseine**) **156223-05-1**; (4 [[2 (1 methyl 2 **pyrrolidinyl**)**ethyl**]**thio**]**phenol**) **191611-76-4**; (n methyl 4 (3 pyridinyl) 3 butenamine) **183288-99-5**; (3 ethynyl 5 (1 methyl 2 pyrrolidinyl)pyridine) **179120-92-4**

CN (1) Sib 1508y; **(2) Rjr 2403**; **(3) Sib 1553a**; (4) Gts 21; **(5) Abt 418**

CO (1) PD; (2) NC; (3) Merck (United States); (4) Taiho (Japan); (5) Abbott (United States)

L161 ANSWER 3 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 1999375791 EMBASE

TI Sex differences in cholinergic analgesia. II: Differing mechanisms in two models of allodynia.

AU Lavand'homme P.M.; Eisenach J.C.

CS Dr. J.C. Eisenach, Department of Anesthesiology, Wake Forest Univ. School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1009, United States. eisenach@wfubmc.edu

SO Anesthesiology, (1999) 91/5 (1455-1461).
Refs: 21
ISSN: 0003-3022 CODEN: ANESAV

CY United States

DT Journal; Article
FS 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Background: Cholinergic agents reduce allodynia after nerve injury in animals and may be useful in the treatment of neuropathic pain. Intrathecally administered neostigmine and neuronal nicotinic agonists are more potent in female than in male rats against acute thermal noxious stimuli. The purpose of this study was to determine whether there is also a sex difference in the antiallodynic effects of intrathecal cholinomimetic agents in two models of allodynia and to test their pharmacologic mechanisms. Methods: Male and female rats with indwelling intrathecal catheters received injections of neostigmine, bethanechol (muscarinic agonist), **RJR-2403** (neuronal nicotinic agonist) alone or with atropine (muscarinic antagonist), **mecamylamine** (nicotinic antagonist), phentolamine (.alpha.-adrenergic antagonist), or saline control. The effect of these agents was determined on mechanical allodynia produced by either intraplantar injection of capsaicin or ligation of spinal nerves. Results: Neostigmine and **RJR-2403** but not bethanechol were more potent in female than in male rats in reducing allodynia after nerve injury, and antagonist studies were also consistent with a nicotinic component to explain this sex difference. Phentolamine did not reverse neostigmine's effect. In contrast, for capsaicin-induced allodynia, neostigmine plus **mecamylamine** but not neostigmine or **RJR -2403** was more potent in female than in male rats. Conclusions: These data demonstrate a sex difference of intrathecal neostigmine after nerve injury-induced allodynia similar to that observed in normal animals that received acute noxious thermal stimulation. However, this sex difference is not universal to all pain models because it was not present after intradermal capsaicin injection, nor is its interaction with spinal noradrenergic mechanisms consistent in all models.
CT Medical Descriptors:
*analgesia
***cholinergic system**
sex difference
allodynia
thermal stimulation
nerve injury
drug potency
nociceptive stimulation
noradrenergic system
pain assessment
nonhuman
male
female
rat
animal experiment
animal model
controlled study
intrathecal drug administration
article
priority journal
Drug Descriptors:
***neostigmine: CB, drug combination**
*neostigmine: CM, drug comparison
*neostigmine: PD, pharmacology
***bethanechol: CB, drug combination**
*bethanechol: CM, drug comparison
*bethanechol: PD, pharmacology
***n methyl 4 (3 pyridinyl) 3 butenamine: CB, drug combination**

*n methyl 4 (3 pyridinyl) 3 butenamine: CM, drug comparison
*n methyl 4 (3 pyridinyl) 3 butenamine: PD, pharmacology
***atropine: CB, drug combination**
*atropine: CM, drug comparison
*atropine: PD, pharmacology
***mecamylamine: CB, drug combination**
***mecamylamine: CM, drug comparison**
***mecamylamine: PD, pharmacology**
***phentolamine: CB, drug combination**
*phentolamine: CM, drug comparison
*phentolamine: PD, pharmacology
capsaicin
RN (neostigmine) 114-80-7, 588-17-0, 59-99-4, 8048-84-8; (bethanechol) 590-63-6, 674-38-4, 91609-06-2; (n methyl 4 (3 pyridinyl) 3 butenamine) **183288-99-5**; (atropine) 51-55-8, 55-48-1; (**mecamylamine**) **60-40-2, 826-39-1**; (phentolamine) 50-60-2, 73-05-2; (capsaicin) 404-86-4
CN **(1) Rjr 2403**
CO (1) Reynolds Tobacco (United States); Gensia (United States); Research Biochemicals (United States); Sigma (United States)

L161 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1999375790 EMBASE
TI Sex differences in cholinergic analgesia I: A supplemental nicotinic mechanism in normal females.
AU Chiari A.; Tobin J.R.; Pan H.-L.; Hood D.D.; Eisenach J.C.
CS Dr. J.C. Eisenach, Department of Anesthesiology, Wake Forest Univ. School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1009, United States. eisenach@wfubmc.edu
SO Anesthesiology, (1999) 91/5 (1447-1454).
Refs: 35
ISSN: 0003-3022 CODEN: ANESAV
CY United States
DT Journal; Article
FS 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Background: Cholinergic agents produce analgesia after systemic and intrathecal administration. A retrospective review showed that intrathecal neostigmine was more potent in women than in men, suggesting a sex difference in this response. The purpose of this study was to determine whether such a sex difference exists in normal rats and to examine the pharmacologic mechanisms that underlie this difference. Methods: Male and female rats with indwelling intrathecal catheters received injections of neostigmine, bethanechol (muscarinic agonist), or **RJR-2403** (neuronal nicotinic agonist) alone or with atropine (muscarinic antagonist), **mecamylamine** (nicotinic antagonist), or phentolamine (.alpha.-adrenergic antagonist) with antinociception determined to a noxious heat stimulus to the hind paw. Time versus subcutaneous paw temperature relationships were defined for males and females. Results: Neostigmine produced dose-dependent antinociception with five times greater potency in female than in male rats. Neostigmine-induced antinociception was reversed in male rats by atropine and unaffected by **mecamylamine**, whereas it was partially reduced by each antagonist alone in females and completely reversed after injection of both. **RJR-2403** was more potent in females than in males, whereas there was no sex difference to bethanechol. Phentolamine partially reversed antinociception from **RJR-2403** in females. Paw temperature increased more rapidly in females than in males for the same lamp intensity. Conclusions: These data demonstrate a large sex difference in antinociception to intrathecal

neostigmine that is primarily the result of a nicotinic component in females. Phentolamine reversal suggests that part of this nicotinic component may rely on spinal norepinephrine release. A better understanding of this sex difference could lead to development of novel pain therapy for women.

CT Medical Descriptors:
*analgesia
***cholinergic system**
sex difference
antinociception
nociceptive stimulation
dose time effect relation
pain assessment
drug potency
nonhuman
male
female
rat
animal experiment
animal model
controlled study
intrathecal drug administration
article
priority journal
Drug Descriptors:
*cholinergic receptor stimulating agent: PD, pharmacology
***neostigmine: CB, drug combination**
*neostigmine: CM, drug comparison
*neostigmine: DO, drug dose
*neostigmine: PD, pharmacology
***bethanechol: CB, drug combination**
*bethanechol: CM, drug comparison
*bethanechol: PD, pharmacology
***n methyl 4 (3 pyridinyl) 3 butenamine: CB, drug combination**
*n methyl 4 (3 pyridinyl) 3 butenamine: CM, drug comparison
*n methyl 4 (3 pyridinyl) 3 butenamine: DO, drug dose
*n methyl 4 (3 pyridinyl) 3 butenamine: PD, pharmacology
***atropine: CB, drug combination**
*atropine: CM, drug comparison
*atropine: PD, pharmacology
***mecamylamine: CB, drug combination**
***mecamylamine: CM, drug comparison**
***mecamylamine: PD, pharmacology**
phentolamine: CB, drug combination
phentolamine: CM, drug comparison
phentolamine: PD, pharmacology

RN (neostigmine) 114-80-7, 588-17-0, 59-99-4, 8048-84-8; (bethanechol) 590-63-6, 674-38-4, 91609-06-2; (n methyl 4 (3 pyridinyl) 3 butenamine) **183288-99-5**; (atropine) 51-55-8, 55-48-1; (**mecamylamine**) **60-40-2, 826-39-1**; (phentolamine) 50-60-2, 73-05-2

CN **(1) Rjr 2403**

CO (1) Reynolds Tobacco (United States); Gensia (United States); Research Biochemicals (United States); Sigma (United States)

=> fil reg
FILE 'REGISTRY' ENTERED AT 11:00:07 ON 04 MAR 2003

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 MAR 2003 HIGHEST RN 496764-40-0
DICTIONARY FILE UPDATES: 2 MAR 2003 HIGHEST RN 496764-40-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

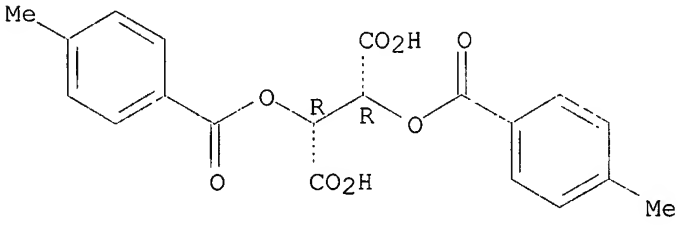
=> d ide can tot

L165 ANSWER 1 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 391624-59-2 REGISTRY
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (3E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H18 O8 . C10 H14 N2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 32634-66-5
CMF C20 H18 O8

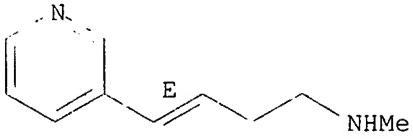
Absolute stereochemistry.



CM 2

CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:112680

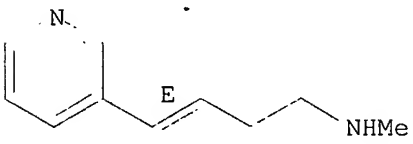
REFERENCE 2: 136:112679

L165 ANSWER 2 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 355114-70-4 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H14 N2 . C4 H6 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 15585-43-0
CMF C10 H14 N2

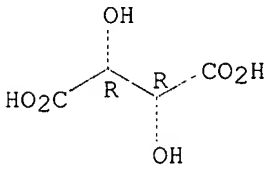
Double bond geometry as shown.



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

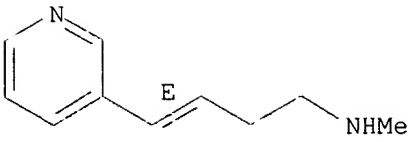
REFERENCE 1: 135:175425

L165 ANSWER 3 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 220662-95-3 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H14 N2 . C2 H2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

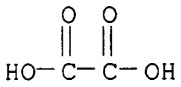
CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



CM 2

CRN 144-62-7
CMF C2 H2 O4



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

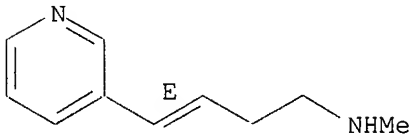
REFERENCE 1: 130:177543

L165 ANSWER 4 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 196399-55-0 REGISTRY
CN Carbamic acid, ethyl-, compd. with (E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (E)-, mono(ethylcarbamate) (9CI)
FS STEREOSEARCH
MF C10 H14 N2 . C3 H7 N O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

CM 1

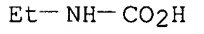
CRN 15585-43-0
CMF C10 H14 N2

Double bond geometry as shown.



CM 2

CRN 7409-13-4
CMF C3 H7 N O2



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

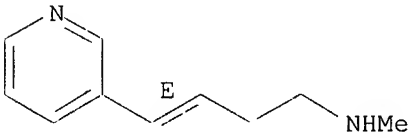
REFERENCE 1: 127:262606

L165 ANSWER 5 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 183288-99-5 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (E)-, (E)-2-butenedioate (1:1)
OTHER NAMES:
CN RJR 2403
FS STEREOSEARCH
MF C10 H14 N2 . C4 H4 O4
SR CA
LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, CSCHEM, DRUGNL, DRUGUPDATES, EMBASE, PHAR, TOXCENTER, USPATFULL

CM 1

CRN 15585-43-0
CMF C10 H14 N2

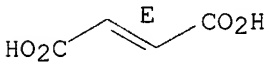
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



17 REFERENCES IN FILE CA (1962 TO DATE)
17 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:131481

REFERENCE 2: 138:83244

REFERENCE 3: 137:304645

REFERENCE 4: 136:221745

REFERENCE 5: 133:168383

REFERENCE 6: 133:130127

REFERENCE 7: 132:313697

REFERENCE 8: 132:216942

REFERENCE 9: 132:216941

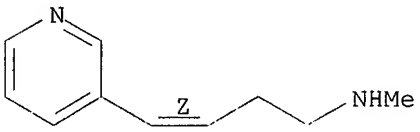
REFERENCE 10: 132:30131

L165 ANSWER 6 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 180915-56-4 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (Z)-, (E)-2-butenedioate (1:2)
FS STEREOSEARCH
MF C10 H14 N2 . 2 C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 1129-68-6
CMF C10 H14 N2

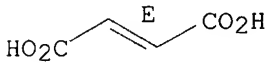
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:185904

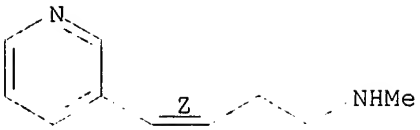
REFERENCE 2: 125:185891

L165 ANSWER 7 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 180915-55-3 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (Z)-, (E)-2-butenedioate (1:1)
FS STEREOSEARCH
MF C10 H14 N2 . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

CRN 1129-68-6
CMF C10 H14 N2

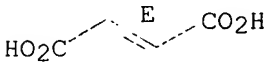
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 133:317546

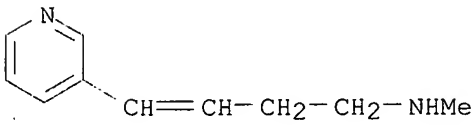
REFERENCE 2: 125:185904

REFERENCE 3: 125:185891

L165 ANSWER 8 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 180740-80-1 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (E)-2-butenedioate (1:2)
FS STEREOSEARCH
MF C10 H14 N2 . 2 C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

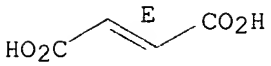
CRN 538-79-4
CMF C10 H14 N2



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



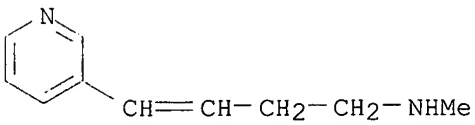
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 125:185907

L165 ANSWER 9 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 109476-14-4 REGISTRY
CN Metanicotine, picrate (6CI) (CA INDEX NAME)
MF C10 H14 N2 . C6 H3 N3 O7
SR CAOLD
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)

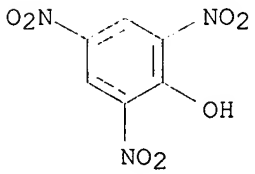
CM 1

CRN 538-79-4
CMF C10 H14 N2



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7

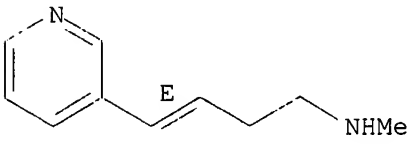


1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L165 ANSWER 10 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 15585-43-0 REGISTRY
CN **3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3E)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (E)-**
CN Pyridine, 3-[4-(methylamino)-1-butenyl]-, (E)- (8CI)
OTHER NAMES:
CN **(3E)-N-Methyl-4-(3-pyridinyl)-3-buten-1-amine**
CN (E)-Metanicotine
CN trans-Metanicotine
FS STEREOSEARCH
MF **C10 H14 N2**
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, DRUGUPDATES,

TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

20 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
20 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:14014

REFERENCE 2: 136:112680

REFERENCE 3: 135:376774

REFERENCE 4: 135:175425

REFERENCE 5: 134:42065

REFERENCE 6: 133:317546

REFERENCE 7: 133:237818

REFERENCE 8: 132:161263

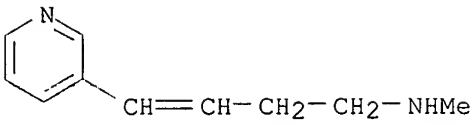
REFERENCE 9: 131:331997

REFERENCE 10: 131:194296

L165 ANSWER 11 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 5960-10-1 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (2R,3R)-2,3-dihydroxybutanedioate (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate
CN Pyridine, 3-[4-(methylamino)-1-butenyl]-, tartrate (7CI, 8CI)
OTHER NAMES:
CN Metanicotine, tartrate
FS STEREOSEARCH
MF C10 H14 N2 . x C4 H6 O6
LC STN Files: CA, CAOLD, CAPLUS

CM 1

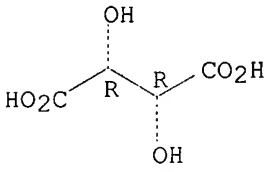
CRN 538-79-4
CMF C10 H14 N2



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



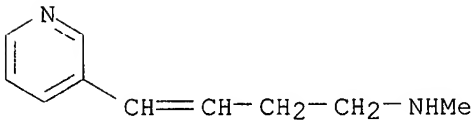
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 65:41767

L165 ANSWER 12 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 4334-83-2 REGISTRY
CN Pyridine, 3-[4-(methylamino)-1-butenyl]-, tartrate (1:1) (8CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H14 N2 . C4 H6 O6
LC STN Files: CA, CAOLD, CAPLUS

CM 1

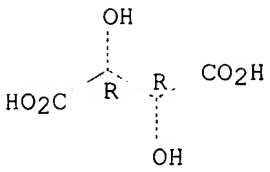
CRN 538-79-4
CMF C10 H14 N2



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



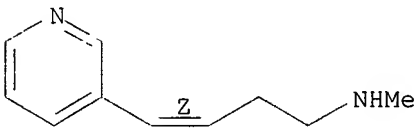
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 63:102250

REFERENCE 2: 63:102249

L165 ANSWER 13 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 1129-68-6 REGISTRY
CN **3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (3Z)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **3-Buten-1-amine, N-methyl-4-(3-pyridinyl)-, (Z)-**
CN Pyridine, 3-[4-(methylamino)-1-butenyl]-, (Z)- (8CI)
OTHER NAMES:
CN (Z)-Metanicotine
CN cis-Metanicotine
FS STEREOSEARCH
MF **C10 H14 N2**
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 133:317546

REFERENCE 2: 130:177543

REFERENCE 3: 129:260345

REFERENCE 4: 125:185907

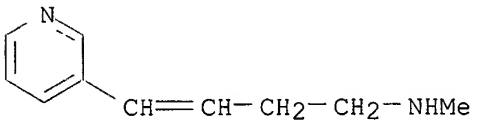
REFERENCE 5: 125:185904

REFERENCE 6: 125:185891

REFERENCE 7: 86:715

REFERENCE 8: 84:130204

L165 ANSWER 14 OF 14 REGISTRY COPYRIGHT 2003 ACS
RN 538-79-4 REGISTRY
CN 3-Buten-1-amine, N-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Metanicotine (6CI)**
CN Pyridine, 3-[4-(methylamino)-1-butenyl]- (7CI, 8CI)
FS 3D CONCORD
MF C10 H14 N2
CI COM
LC STN Files: ADISINSIGHT, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, DDFU, DRUGU, EMBASE, IPA, MEDLINE, NAPRALERT, RTECS*, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

44 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
44 REFERENCES IN FILE CAPLUS (1962 TO DATE)
18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:83230

REFERENCE 2: 136:288399

REFERENCE 3: 135:340964

REFERENCE 4: 133:168383

REFERENCE 5: 130:177139

REFERENCE 6: 120:2316

REFERENCE 7: 112:118575

REFERENCE 8: 103:220691

REFERENCE 9: 102:144648

REFERENCE 10: 101:145811

=> fil medline
FILE 'MEDLINE' ENTERED AT 11:08:14 ON 04 MAR 2003

FILE LAST UPDATED: 2 MAR 2003 (20030302/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html

for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L176 ANSWER 1 OF 22 MEDLINE
AN 2002629290 MEDLINE
DN 22251085 PubMed ID: 12364511
TI Pharmacology of nicotinic receptors in preBotzinger complex that mediate modulation of respiratory pattern.
AU Shao Xuesi M; Feldman Jack L
CS Department of Neurobiology, UCLA School of Medicine, Los Angeles, California 90095-1763, USA.. mshao@ucla.edu
NC HL-40959 (NHLBI)
SO JOURNAL OF NEUROPHYSIOLOGY, (2002 Oct) 88 (4) 1851-8.
Journal code: 0375404. ISSN: 0022-3077.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20021022
Last Updated on STN: 20021213
Entered Medline: 20021125
AB Nicotine regulates respiratory pattern by modulating excitatory neurotransmission affecting inspiratory neurons within the preBotzinger Complex (preBotC). The nicotinic acetylcholine receptor (nAChR) subtypes mediating these effects are unknown. Using a medullary slice preparation from neonatal rat, we recorded spontaneous respiratory-related rhythm from the hypoglossal nerve (XIIn) and patch-clamped inspiratory neurons in the preBotC simultaneously. The alpha7 nAChR antagonists alpha-bungarotoxin or methyllycaconitine (MLA) had little effect on the actions of low concentrations of nicotine (0.5 microM), which included an increase in respiratory frequency; a decrease in amplitude of XIIn inspiratory bursts; a tonic inward current associated with an increase in membrane noise; an increase in the frequency and amplitude of spontaneous excitatory postsynaptic currents (sEPSCs), and; a decrease in the amplitude of inspiratory drive current in voltage-clamped preBotC inspiratory neurons. These nicotinic actions were completely reversed by dihydro-beta-erythroidine (DH-beta-E) or hexamethonium and reduced by D-tubocurarine. Comparable concentrations of **RJR-2403** (0.5-1 microM), an agonist selective for alpha4beta2 nAChRs, increased respiratory frequency to 186% and decreased the amplitude of XIIn inspiratory bursts to 83% of baseline. In voltage-clamped preBotC inspiratory (including pacemaker) neurons, **RJR-2403** induced a tonic inward current of -15.2 pA associated with an increase in membrane noise, increased the frequency to 157% and amplitude to 106% of spontaneous EPSCs, and decreased the amplitude of inspiratory drive current to 80% of baseline. MLA had little effect on **RJR-2403** actions, while DH-beta-E completely reversed them. These results suggest that the predominant subtype of nAChRs in preBotC in neonatal rats that mediates the modulation of respiratory pattern by low concentrations of nicotine is an alpha4beta2 combination and not an alpha7 subunit homomer. We do not exclude the possibility that co-assembly of alpha4beta2 with other subunits or other nAChR subtypes are also expressed in preBotC neurons. The parallel changes in the cellular and systems level responses induced by different nicotinic agonists and antagonists support the idea that modulation of excitatory neurotransmission affecting preBotC inspiratory neurons is a mechanism underlying the cholinergic regulation of respiratory pattern (). This study provides a useful model system for evaluating potential therapeutic cholinergic agents for their respiratory

effects and side effects.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Excitatory Postsynaptic Potentials: DE, drug effects
Excitatory Postsynaptic Potentials: PH, physiology
Hypoglossal Nerve: PH, physiology
Nicotine: PD, pharmacology
Nicotinic Agonists: PD, pharmacology
Nicotinic Antagonists: PD, pharmacology
Rats
Rats, Sprague-Dawley
***Receptors, Nicotinic: PH, physiology**
Respiratory Center: DE, drug effects
***Respiratory Center: PH, physiology**
*Respiratory Mechanics: PH, physiology
RN 54-11-5 (Nicotine)
CN 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic)

L176 ANSWER 2 OF 22 MEDLINE
AN 2002416119 MEDLINE
DN 22093066 PubMed ID: 12098588
TI Characterization of functional nicotinic acetylcholine receptors involved in catecholamine release from the isolated rat adrenal gland.
AU Yokotani Kunihiko; Okada Shoshiro; Nakamura Kumiko
CS Department of Pharmacology, Kochi Medical School, Nankoku, Kochi, 783-8505, Japan. yakotani@dtn.am400gw.kochi-ms.ac.jp
SO EUROPEAN JOURNAL OF PHARMACOLOGY, (2002 Jun 20) 446 (1-3) 83-7. Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20020813
Last Updated on STN: 20030109
Entered Medline: 20030108
AB We tried to characterize nicotinic acetylcholine receptors involved in the release of catecholamines from the rat adrenal gland. The isolated adrenal gland was retrogradely perfused via the adrenal vein with Krebs-Ringer solution at a flow rate of 0.5 ml/min. Endogenous catecholamines, adrenaline and noradrenaline, released into the perfusate were electrochemically measured using high-performance liquid chromatography. (-)-Nicotine (3 x 10(-6)-3 x 10(-5) M) evoked the release of catecholamines (adrenaline >> noradrenaline) in a concentration-dependent manner. The (-)-nicotine (10(-5) M)-induced release of catecholamines was effectively attenuated by mecamylamine (10(-7) and 10(-6) M) (a relatively selective antagonist of alpha3beta4 nicotinic receptors), but not influenced by alpha-bungarotoxin (3 x 10(-7) M) (an antagonist of alpha7 nicotinic receptors) and dihydro-beta-erythroidine (10(-5) M) (a relatively selective antagonist of alpha4beta2 nicotinic receptors). (+/-)-Epibatidine (3 x 10(-7) and 10(-6) M) (a non-selective nicotinic receptor agonist), (-)-cytisine (10(-5) and 10(-4) M) (an agonist of beta4 nicotinic receptors) and (+/-)-2-(3-pyridinyl)-1-azabicyclo(2.2.2)octane (RJR-2429) (10(-5) M) (a putative agonist of alpha3beta4 nicotinic receptors) effectively evoked the release of catecholamines (adrenaline >> noradrenaline), while (E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine (**RJR-2403**) (up to 10(-4) M) (a selective agonist of alpha4beta2 nicotinic receptors) had no effect. The efficacies of these agonists are as follows: (+/-) epibatidine >> RJR-2429>(-)-cytisine>(-)-nicotine >> **RJR-2403**. These results suggest that alpha3beta4 nicotinic receptors are involved in the release of catecholamines from the rat adrenal gland.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't

*Adrenal Glands: ME, metabolism
*Catecholamines: ME, metabolism
Epinephrine: ME, metabolism
Nicotine: PD, pharmacology
Nicotinic Agonists: PD, pharmacology
Nicotinic Antagonists: PD, pharmacology
Rats
Rats, Wistar
Receptors, Nicotinic: DE, drug effects
***Receptors, Nicotinic: PH, physiology**
Stomach: ME, metabolism
RN 51-43-4 (Epinephrine); 54-11-5 (Nicotine)
CN 0 (Catecholamines); 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic)

L176 ANSWER 3 OF 22 MEDLINE
AN 2002415163 MEDLINE
DN 22159343 PubMed ID: 12170059
TI Nicotinic acetylcholine receptor regulation of spinal norepinephrine release.
AU Li Xinhui; Eisenach James C
CS Department of Anesthesiology and Center for the Study of Pharmacologic Plasticity in the Presence of Pain, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157, USA.
NC GM35523 (NIGMS)
NS41386 (NINDS)
SO ANESTHESIOLOGY, (2002 Jun) 96 (6) 1450-6.
Journal code: 1300217. ISSN: 0003-3022.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200208
ED Entered STN: 20020810
Last Updated on STN: 20020829
Entered Medline: 20020827
AB BACKGROUND: Neuronal nicotinic acetylcholine receptor (nAChR) agonists produce antinociception in animals. nAChRs exist almost exclusively on presynaptic terminals in the central nervous system and stimulate neurotransmitter release. This study tested whether nAChR agonists stimulate spinal release of the neurotransmitter norepinephrine either by direct actions on noradrenergic terminals or indirectly by stimulating release of other neurotransmitters to induce norepinephrine release. METHODS: Adult male rats were anesthetized and microdialysis probes inserted in the L2-L4 dermatomes of the spinal cord. Probes were perfused with artificial cerebrospinal fluid containing nicotine, the specific alpha(4)beta(2*) nAChR agonist **metanicotine**, or nicotine plus nAChR antagonists and norepinephrine measured in the microdialysates. The effects of specific glutamate receptor antagonists and nitric oxide synthase inhibitors were also examined. To determine direct effects on noradrenergic terminals, synaptosomes were prepared from spinal cord and incubated with nAChR agonists and antagonists. RESULTS: Both nicotine and **metanicotine** induced norepinephrine release in spinal microdialsyates, an effect reduced by nicotinic antagonists but not glutamate antagonists or nitric oxide synthase inhibitors. Both of the nicotinic agonists stimulated norepinephrine release in synaptosomes, and the effect of **metanicotine** was blocked at lower concentrations of alpha(4)beta(2*)- than alpha(7*)-preferring nAChR antagonists. CONCLUSION: These results suggest that one mechanism by which nAChR agonists act for analgesia is to stimulate spinal norepinephrine release. They do so by actions on alpha(4)beta(2*) nAChRs, and perhaps other subtypes, most likely located on noradrenergic terminals, rather than by indirectly stimulating norepinephrine release through glutamate release or

nitric oxide synthesis.
CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
Analgesia
Azetidines: PD, pharmacology
Desipramine: PD, pharmacology
Microdialysis
Nitric Oxide: PH, physiology
*Norepinephrine: SE, secretion
Pyridines: PD, pharmacology
Rats
Rats, Sprague-Dawley
Receptors, Glutamate: PH, physiology
***Receptors, Nicotinic: PH, physiology**
Spinal Cord: PH, physiology
***Spinal Cord: SE, secretion**
Synaptosomes: DE, drug effects
RN 10102-43-9 (Nitric Oxide); 50-47-5 (Desipramine); 51-41-2 (Norepinephrine)
CN 0 (5-(2-azetidinylmethoxy)-2-chloropyridine); 0 (Azetidines); 0 (Pyridines); 0 (Receptors, Glutamate); 0 (Receptors, Nicotinic)

L176 ANSWER 4 OF 22 MEDLINE
AN 2002322935 MEDLINE
DN 22061007 PubMed ID: 12065705
TI Alpha4beta2 nicotinic acetylcholine receptor activation ameliorates impairment of spontaneous alternation behavior in stroke-prone spontaneously hypertensive rats, an animal model of attention deficit hyperactivity disorder.
AU Ueno Ken-Ichi; Togashi Hiroko; Matsumoto Machiko; Ohashi Satoshi; Saito Hideya; Yoshioka Mitsuhiro
CS Department of Pharmacology, Hokkaido University Graduate School of Medicine, Kita-15, Nishi-7, Kita-ku, Sapporo 060-8638, Japan.. ken-ueno@med.hokudai.ac.jp
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2002 Jul) 302 (1) 95-100.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020615
Last Updated on STN: 20020713
Entered Medline: 20020712
AB The objective of the present study was to elucidate the role of nicotine in impairment of spontaneous alternation behavior of juvenile stroke-prone spontaneously hypertensive rats (SHRSP), an animal model of attention deficit hyperactivity disorder (ADHD). Spontaneous alternation behavior assessed by a Y-maze task was significantly lower, and total arm entries were significantly higher in SHRSP than in genetic control Wistar-Kyoto rats. Nicotine (0.1-1 mg/kg, s.c.) dose dependently improved the spontaneous alternation deficit without affecting total arm entries in SHRSP. Nicotine-induced (1 mg/kg, s.c.) improvement was significantly abolished by the centrally acting nicotinic acetylcholine receptor (nAChR) antagonist mecamylamine (1 mg/kg, i.p.), but not by peripherally acting hexamethonium (5 mg/kg, i.p.), suggesting that nicotine-induced improvement is mediated via central nAChR. The alpha4beta2 nAChR antagonist dihydro-beta-erythroidine (3-10 mg/kg, i.p.) dose dependently counteracted nicotine-induced improvement of spontaneous alternation in SHRSP, whereas the alpha7 nAChR antagonist methyllycaconitine (3-10 mg/kg, i.p.) did not. In addition, the alpha4beta2 nAChR agonist **RJR-2403** (N-methyl-4-(3-pyridinyl)-3-butene-1-amine; 1-10 mg/kg, s.c.) dose dependently and significantly improved the spontaneous alternation deficit. These findings revealed that nicotine improved spontaneous

alternation behavior in SHRSP via the activation of alpha4beta2, but not alpha7, nAChR. Thus, the alpha4beta2 nAChR mechanism might be responsible for the spontaneous alternation deficit in juvenile SHRSP, an animal model of ADHD. This evidence indicates the possibility that selective alpha4beta2 nAChR agonists might be useful for treating attentional dysfunction in ADHD.

CT Check Tags: Animal
***Attention Deficit Disorder with Hyperactivity: DT, drug therapy**
***Attention Deficit Disorder with Hyperactivity: GE, genetics**
Attention Deficit Disorder with Hyperactivity: PX, psychology
***Behavior, Animal: DE, drug effects**
Central Nervous System Agents: PD, pharmacology
Dihydro-beta-Erythroidine: PD, pharmacology
Dose-Response Relationship, Drug
Hexamethonium: PD, pharmacology
*Hypertension: GE, genetics
*Hypertension: PX, psychology
Mecamylamine: PD, pharmacology
Nicotine: PD, pharmacology
***Nicotinic Agonists: PD, pharmacology**
Nicotinic Antagonists: PD, pharmacology
Peripheral Nervous System: DE, drug effects
Rats
Rats, Inbred SHR
Rats, Inbred WKY
***Receptors, Nicotinic: DE, drug effects**

RN 23255-54-1 (Dihydro-beta-Erythroidine); 54-11-5 (Nicotine); 60-26-4 (Hexamethonium); 60-40-2 (Mecamylamine)

CN 0 (Central Nervous System Agents); 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic); 0 (alpha-bungarotoxin receptor); 0 (nicotinic receptor alpha4beta2)

L176 ANSWER 5 OF 22 MEDLINE

AN 2002225167 MEDLINE

DN 21959241 PubMed ID: 11961083

TI Enhanced inhibition of a mutant neuronal nicotinic acetylcholine receptor by agonists: protection of function by (E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine (TC-2403).

AU Papke Roger L

CS Department of Pharmacology and Therapeutics, University of Florida, Gainesville, Florida 32610-0267, USA.. rpapke@college.med.ufl.edu

NC NS32888-02 (NINDS)

SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (2002 May) 301 (2) 765-73.
Journal code: 0376362. ISSN: 0022-3565.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200205

ED Entered STN: 20020419
Last Updated on STN: 20020514
Entered Medline: 20020513

AB Inhibition of neuronal nicotinic receptors can be regulated by sequence in the beta subunit second transmembrane domain (TM2). The incorporation of a beta4(6'F10'T) subunit, which contains sequence from the muscle beta subunit at the TM2 6' and 10' positions of the neuronal beta4 subunit, increases the loss of receptor responsiveness after the application of acetylcholine (ACh), nicotine, or 3-(2,4-dimethoxybenzylidene)-anabaseine (DMXB), an alpha7-selective partial agonist. Inhibition of receptor responsiveness following agonist exposure may occur through either an enhancement of desensitization, increased channel block by an agonist, or alternatively via allosteric modulation. Although DMXB produces very

little activation of either alpha3beta4 or alpha3beta4(6'F10'T) receptors, DMXB shows an enhanced use-and voltage-dependent inhibition of alpha3beta4(6'F10'T) receptors compared with wild-type. In contrast, the alpha4beta2-selective agonist (E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine (TC-2403, previously identified as **RJR-2403**) shows increased activation of alpha3beta4(6'F10'T) receptors compared with alpha3beta4 receptors (as related to ACh activation) but with no significant increase in antagonist activity. The interaction between the binding of local anesthetics and the functional inhibition produced by these agonists was evaluated. The binding of the local anesthetics to their inhibitory sites does not affect inhibitory effects of DMXB and nicotine. However, TC-2403 can protect receptor function from the inhibitory effects of other agonists, suggesting that TC-2403, as well as agonists that cause inhibition, may be binding to an allosteric site, either promoting or inhibiting channel opening. The ability of TC-2403 to protect receptor function from agonist-induced inhibition may point toward valuable new combination drug therapies.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Acetylcholine: PD, pharmacology
Amino Acid Sequence
Benzylidene Compounds: PD, pharmacology
Electrophysiology
Molecular Sequence Data
Mutagenesis, Site-Directed
***Neurons: ME, metabolism**
Nicotine: AA, analogs & derivatives
***Nicotine: PD, pharmacology**
***Nicotinic Agonists: PD, pharmacology**
***Nicotinic Antagonists: PD, pharmacology**
Oocytes: DE, drug effects
Oocytes: ME, metabolism
Pyridines: PD, pharmacology
Rats
Receptors, Nicotinic: DE, drug effects
Receptors, Nicotinic: GE, genetics
***Receptors, Nicotinic: ME, metabolism**
Sequence Homology, Amino Acid
Transfection
Xenopus laevis

RN 156223-05-1 (3-(2,4-dimethoxybenzylidene)anabaseine); 51-84-3 (Acetylcholine); **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)

CN 0 (Benzylidene Compounds); 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Pyridines); 0 (Receptors, Nicotinic); 0 (nicotinic receptor alpha3beta4)

L176 ANSWER 6 OF 22 MEDLINE
AN 2002067577 MEDLINE
DN 21651293 PubMed ID: 11794523
TI Synthesis of (+/-)-methyl-(1-aryl-4-pyridin-3-yl-but-3-enyl)-amines.
AU Jang J; Sin K S; Park H
CS College of Pharmacy, Kangwon National University, Chunchon, Korea.
SO ARCHIVES OF PHARMACAL RESEARCH, (2001 Dec) 24 (6) 503-7.
Journal code: 8000036. ISSN: 0253-6269.
CY KOREA (SOUTH)
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020125
Last Updated on STN: 20020625
Entered Medline: 20020624

AB trans-**Metanicotine**, a subtype (alpha4beta2)-selective ligand for neuronal nicotinic acetylcholine receptor, is under clinical phase for

Alzheimer's disease. An efficient synthetic route for (+/-)-methyl-(1-aryl-4-pyridin-3-yl-but-3-enyl)-amines, derivatives of trans-**metanicotine**, was explored. Allylation reaction of aryl aldimines with allylmagnesium bromide in THF gave (+/-)-methyl-(1-aryl-but-3-enyl)-amines. Protection of the amines with the Boc group and following Heck reaction of the N-Boc amines with 3-bromopyridine gave (+/-)-methyl-(1-aryl-4-pyridin-3-yl-but-3-enyl)-carbamic acid tert-butyl esters. Deprotection of the N-Boc group in aqueous 1N-HCI solution gave the titled amines in good yields. Thus, trans-**metanicotine** analogues modified at the a-position of the methylamino group with aryl groups were obtained in 5 steps.

CT Check Tags: Support, Non-U.S. Gov't
Nicotine: AA, analogs & derivatives
***Nicotine: CS, chemical synthesis**
***Nicotinic Agonists: CS, chemical synthesis**

RN **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)

CN 0 (Nicotinic Agonists)

L176 ANSWER 7 OF 22 MEDLINE

AN 2002048957 MEDLINE

DN 21634391 PubMed ID: 11772288

TI The therapeutic potential of nicotinic acetylcholine receptor agonists for pain control.

AU Decker M W; Meyer M D; Sullivan J P

CS Dept. 4N5, Building AP-9A/3, 100 Abbott Park Rd., Abbott Park, IL 60064-6125, USA.. michael.w.decker@abbott.com

SO EXPERT OPINION ON INVESTIGATIONAL DRUGS, (2001 Oct) 10 (10) 1819-30. Ref: 96
Journal code: 9434197. ISSN: 1354-3784.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 200202

ED Entered STN: 20020125
Last Updated on STN: 20020301
Entered Medline: 20020228

AB Due to the limitations of currently available analgesics, a number of novel alternatives are currently under investigation, including neuronal nicotinic acetylcholine receptor (nAChR) agonists. During the 1990s, the discovery of the antinociceptive properties of the potent nAChR agonist epibatidine in rodents sparked interest in the analgesic potential of this class of compounds. Although epibatidine also has several mechanism-related toxicities, the identification of considerable nAChR diversity suggested that the toxicities and therapeutic actions of the compound might be mediated by distinct receptor subtypes. Consistent with this view, a number of novel nAChR agonists with antinociceptive activity and improved safety profiles in preclinical models have now been identified, including A-85380, ABT-594, DBO-83, SIB-1663 and **RJR -2403**. Of these, ABT-594 is the most advanced and is currently in Phase II clinical evaluation. Nicotinically-mediated antinociception has been demonstrated in a variety of rodent pain models and is likely mediated by the activation of descending inhibitory pathways originating in the brainstem with the predominant high-affinity nicotine site in brain, the alpha4beta2 subtype, playing a critical role. Thus, preclinical findings suggest that nAChR agonists have the potential to be highly efficacious treatments in a variety of pain states. However, clinical proof-of-principle studies will be required to determine if nAChR agonists are active in pathological pain.

CT Check Tags: Animal; Human
Nicotinic Agonists: AE, adverse effects

Nicotinic Agonists: PK, pharmacokinetics
Nicotinic Agonists: PD, pharmacology
***Nicotinic Agonists: TU, therapeutic use**
***Pain: DT, drug therapy**
Pain Measurement: DE, drug effects
***Receptors, Nicotinic: DE, drug effects**
CN 0 (Nicotinic Agonists); 0 (Receptors, Nicotinic)

L176 ANSWER 8 OF 22 MEDLINE
AN 2001037888 MEDLINE
DN 20416188 PubMed ID: 10958888
TI Characterization of nicotinic acetylcholine receptor-mediated noradrenaline release from the isolated rat stomach.
AU Yokotani K; Wang M; Okada S; Murakami Y; Hirata M
CS Department of Pharmacology, Kochi Medical School, Nankoku, 783-8505, Kochi, Japan.. yokotani@dtn.am400gw.kochi-ms.ac.jp
SO EUROPEAN JOURNAL OF PHARMACOLOGY, (2000 Aug 25) 402 (3) 223-9. Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001128
AB We characterized nicotinic acetylcholine receptor-mediated noradrenaline release from the isolated, vascularly perfused rat stomach. The stomach was perfused via the coeliac artery with Krebs-Ringer solution at a constant flow rate of 4 ml per minute. Endogenous noradrenaline released into the perfusate was electrochemically measured using high-performance liquid chromatography. Nicotinic receptor agonists were applied once into the perfusion medium for 2 min and nicotinic receptor antagonists were administered throughout the experiments. The (-)-nicotine (3x10(-5) M)-induced noradrenaline release was abolished by tetrodotoxin and hexamethonium and partially blocked by dihydro-beta-erythroidine (up to 10(-5) M) (a relatively selective antagonist of alpha4beta2 nicotinic receptors) and abolished by mecamylamine (10(-5) M) (a relatively selective antagonist of alpha3beta4 nicotinic receptors), but not influenced by alpha-bungarotoxin (3x10(-7) M) or alpha-conotoxin ImI (10(-6) M) (antagonists of alpha7 nicotinic receptors). (+/-)-Epibatidine (3x10(-7) M) (a very potent, but non-selective agonist) and (-)-cytisine (3x10(-4) M) (an agonist of beta4 nicotinic receptors) effectively evoked the release of noradrenaline, while (E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine (**RJR-2403**) (up to 10(-4) M) (an agonist of alpha4beta2 nicotinic receptors) had no effect. The potency of these agonists was as followed; (+/-)-epibatidine>>(-)-nicotine>(-)-cytisine>>> **RJR -2403**. These results are compatible with the published view that alpha3beta4 nicotinic receptors are predominant in other parts of the autonomic nervous system. These receptors (probably located on the gastric sympathetic ganglia) are involved in the release of noradrenaline from the rat stomach.
CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't
Catecholamines: ME, metabolism
Chromatography, High Pressure Liquid
Hexamethonium Compounds: PD, pharmacology
Nicotine: PD, pharmacology
Nicotinic Agonists: PD, pharmacology
Nicotinic Antagonists: PD, pharmacology
*Norepinephrine: ME, metabolism
Rats
Rats, Wistar
Receptors, Nicotinic: DE, drug effects

***Receptors, Nicotinic: PH, physiology**
Stomach: DE, drug effects
*Stomach: ME, metabolism
Tetrodotoxin: PD, pharmacology
RN 4368-28-9 (Tetrodotoxin); 51-41-2 (Norepinephrine); 54-11-5 (Nicotine)
CN 0 (Catecholamines); 0 (Hexamethonium Compounds); 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic)

L176 ANSWER 9 OF 22 MEDLINE
AN 2001026479 MEDLINE
DN 20352944 PubMed ID: 10896048
TI A concise synthetic pathway for trans-**metanicotine** analogues.
AU Park H; Jang J; Sin K S
CS College of Pharmacy, Kangwon National University, Chunchon, Korea.. haeilp@cc.kangwon.ac.kr
SO ARCHIVES OF PHARMACAL RESEARCH, (2000 Jun) 23 (3) 202-5.
Journal code: 8000036. ISSN: 0253-6269.
CY KOREA (SOUTH)
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001114
AB A convenient pathway for synthesis of trans-**metanicotine** analogues was developed. trans-**Metanicotine**, a subtype (alpha4beta2)-selective ligand for neuronal nicotinic acetylcholine receptor, is under clinical phase for Alzheimer's disease. Zn-mediated allylation of allyl bromide and acetaldehyde followed by Heck reaction with 3-bromopyridine gave 5-pyridin-3-yl-pent-4-en-3-ol (2). Tosylation of 5-pyridin-3-yl-pent-4-en-3-ol followed by substitution reaction with methylamine in sealed tube gave methyl-(1-methyl-4-pyridin-3-yl-but-3-enyl)-amine (4) in good yields. Thus, trans-**metanicotine** analogues modified at the alpha-position of the methylamino group with various functional groups can be obtained in 4 steps.
CT ***Nicotine: AA, analogs & derivatives**
Nicotine: CS, chemical synthesis
***Nicotinic Agonists: CS, chemical synthesis**
RN **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)
CN 0 (Nicotinic Agonists)

L176 ANSWER 10 OF 22 MEDLINE
AN 2001009761 MEDLINE
DN 20398086 PubMed ID: 10938478
TI Synthesis and in vivo evaluation of (E)-N-[(11)C]Methyl-4-(3-pyridinyl)-3-butene-1-amine ([(11)C]**metanicotine**) as a nicotinic receptor radioligand.
AU Brown-Proctor C; Snyder S E; Sherman P S; Kilbourn M R
CS Division of Nuclear Medicine, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan 48109-0028, USA.
NC NS24896 (NINDS)
T32-CA09015 (NCI)
SO NUCLEAR MEDICINE AND BIOLOGY, (2000 May) 27 (4) 415-8.
Journal code: 9304420. ISSN: 0969-8051.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001026

AB (E)-N-[(11)C]Methyl-4-(3-pyridinyl)-3-butene-1-amine ([(11)C] **metanicotine**), a high affinity (K(i) = 16 nM) CNS-selective nicotinic agonist, was prepared by the [(11)C]alkylation of the desmethyl precursor with [(11)C]methyl trifluoromethanesulfonate. In vivo distribution studies in mice demonstrated good blood brain permeability but essentially uniform regional brain distribution and no evidence of specific binding to nicotinic cholinergic receptors. Identical results were obtained in an imaging study performed in a monkey brain. Therefore, despite literature reports supporting the use of **metanicotine** as a cognition enhancing nicotinic agonist, (E)-N-[(11)C]methyl-4-(3-pyridinyl)-3-butene-1-amine does not appear to be a suitable candidate for in vivo imaging studies of nicotinic acetylcholine receptors in the mammalian brain.

CT Check Tags: Animal; Female; Support, U.S. Gov't, P.H.S.
Binding, Competitive
Brain Chemistry
*Carbon Radioisotopes: DU, diagnostic use
Macaca nemestrina
Mice
***Nicotine: AA, analogs & derivatives**
Nicotine: ME, metabolism
***Nicotinic Agonists: ME, metabolism**
***Receptors, Nicotinic: AN, analysis**
Tomography, Emission-Computed

RN **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)

CN 0 (Carbon Radioisotopes); 0 (Nicotinic Agonists); 0 (Receptors, Nicotinic)

L176 ANSWER 11 OF 22 MEDLINE

AN 2000312871 MEDLINE

DN 20312871 PubMed ID: 10854263

TI The activation and inhibition of human nicotinic acetylcholine receptor by **RJR-2403** indicate a selectivity for the alpha4beta2 receptor subtype.

AU Papke R L; Webster J C; Lippiello P M; Bencherif M; Francis M M

CS Department of Pharmacology and Therapeutics, University of Florida College of Medicine, Gainesville, Florida, USA.. rpapke@college.med.ufl.edu

NC RO1 NS3288 (NINDS)

SO JOURNAL OF NEUROCHEMISTRY, (2000 Jul) 75 (1) 204-16.
Journal code: 2985190R. ISSN: 0022-3042.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200007

ED Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000717

AB Human nicotinic acetylcholine (ACh) receptor subtypes expressed in Xenopus oocytes were characterized in terms of their activation by the experimental agonist **RJR-2403**. Responses to **RJR-2403** were compared with those evoked by ACh and nicotine. These agonists were also characterized in terms of whether application of the drugs had the effect of producing a residual inhibition that was manifest as a decrease in subsequent control responses to ACh measured 5 min after the washout of the drug. For the activation of alpha4beta2 receptors, **RJR-2403** had an efficacy equivalent to that of ACh and was more potent than ACh. **RJR-2403** was less efficacious than ACh for other human receptor subtypes, suggesting that it is a partial agonist for all these receptors. Nicotine activated peak currents in human alpha4beta2 and alpha3beta2 receptors that were 85 and 50% of the respective ACh maximum responses. Nicotine was an efficacious activator of human alpha7 receptors, with a potency similar to ACh, whereas **RJR-2403** had very low

potency and efficacy for these receptors. At concentrations of <1 mM, **RJR-2403** did not produce any residual inhibition of subsequent ACh responses for any receptor subtype. In contrast, nicotine produced profound residual inhibition of human alpha4beta2, alpha3beta2, and alpha7 receptors with IC(50) values of 150, 200, and 150 microM, respectively. Co-expression of the human alpha5 subunit with alpha3 and beta2 subunits had the effect of producing protracted responses to ACh and increasing residual inhibition by ACh and nicotine but not **RJR-2403**. In conclusion, our results, presented in the context of the complex pharmacology of nicotine for both activating and inhibiting neuronal nicotinic receptor subtypes, suggest that **RJR-2403** will be a potent and relatively selective activator of human alpha4beta2 receptors.

CT Check Tags: Animal; Comparative Study; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Acetylcholine: PD, pharmacology
Electric Conductivity
***Nicotine: AA, analogs & derivatives**
Nicotine: PD, pharmacology
***Nicotinic Agonists: PD, pharmacology**
***Nicotinic Antagonists: PD, pharmacology**
***Receptors, Nicotinic: DE, drug effects**
Receptors, Nicotinic: PH, physiology
Xenopus laevis

RN 51-84-3 (Acetylcholine); **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)

CN 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic)

L176 ANSWER 12 OF 22 MEDLINE

AN 2000017760 MEDLINE

DN 20017760 PubMed ID: 10551598

TI Sex differences in cholinergic analgesia II: differing mechanisms in two models of allodynia.

AU Lavand'homme P M; Eisenach J C

CS Department of Anesthesiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157-1009, USA.

NC GM48085 (NIGMS)

SO ANESTHESIOLOGY, (1999 Nov) 91 (5) 1455-61.
Journal code: 1300217. ISSN: 0003-3022.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199911

ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991124

AB BACKGROUND: Cholinergic agents reduce allodynia after nerve injury in animals and may be useful in the treatment of neuropathic pain. Intrathecally administered neostigmine and neuronal nicotinic agonists are more potent in female than in male rats against acute thermal noxious stimuli. The purpose of this study was to determine whether there is also a sex difference in the antiallodynic effects of intrathecal cholinomimetic agents in two models of allodynia and to test their pharmacologic mechanisms. METHODS: Male and female rats with indwelling intrathecal catheters received injections of neostigmine, bethanechol (muscarinic agonist), **RJR-2403** (neuronal nicotinic agonist) alone or with atropine (muscarinic antagonist), mecamylamine (nicotinic antagonist), phentolamine (alpha-adrenergic antagonist), or saline control. The effect of these agents was determined on mechanical allodynia produced by either intraplantar injection of capsaicin or ligation of spinal nerves. RESULTS: Neostigmine and **RJR-**

2403 but not bethanechol were more potent in female than in male rats in reducing allodynia after nerve injury, and antagonist studies were also consistent with a nicotinic component to explain this sex difference. Phentolamine did not reverse neostigmine's effect. In contrast, for capsaicin-induced allodynia, neostigmine plus mecamylamine but not neostigmine or **RJR-2403** was more potent in female than in male rats. CONCLUSIONS: These data demonstrate a sex difference of intrathecal neostigmine after nerve injury-induced allodynia similar to that observed in normal animals that received acute noxious thermal stimulation. However, this sex difference is not universal to all pain models because it was not present after intradermal capsaicin injection, nor is its interaction with spinal noradrenergic mechanisms consistent in all models.

CT Check Tags: Animal; Comparative Study; Female; Male; Support, U.S. Gov't, P.H.S.
Analgesics: AD, administration & dosage
*Analgesics: PD, pharmacology
Capsaicin: TO, toxicity
Cholinergic Agents: AD, administration & dosage
*Cholinergic Agents: PD, pharmacology
Injections, Spinal
Ligation
Muscarinic Agonists: AD, administration & dosage
Muscarinic Agonists: PD, pharmacology
Muscarinic Antagonists: AD, administration & dosage
Muscarinic Antagonists: PD, pharmacology
Neostigmine: AD, administration & dosage
*Neostigmine: PD, pharmacology
Nicotinic Agonists: AD, administration & dosage
Nicotinic Agonists: PD, pharmacology
Nicotinic Antagonists: AD, administration & dosage
Nicotinic Antagonists: PD, pharmacology
Pain: CI, chemically induced
***Pain: DT, drug therapy**
Pain Measurement
Rats
Rats, Sprague-Dawley
Sex Factors
Spinal Nerves: PH, physiology
RN 404-86-4 (Capsaicin); 59-99-4 (Neostigmine)
CN 0 (Analgesics); 0 (Cholinergic Agents); 0 (Muscarinic Agonists); 0 (Muscarinic Antagonists); 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists)

L176 ANSWER 13 OF 22 MEDLINE
AN 2000017759 MEDLINE
DN 20017759 PubMed ID: 10551597
TI Sex differences in cholinergic analgesia I: a supplemental nicotinic mechanism in normal females.
AU Chiari A; Tobin J R; Pan H L; Hood D D; Eisenach J C
CS Department of Anesthesiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157-1009, USA.
NC GM35523 (NIGMS)
GM48085 (NIGMS)
M01 RR07122 (NCRR)
SO ANESTHESIOLOGY, (1999 Nov) 91 (5) 1447-54.
Journal code: 1300217. ISSN: 0003-3022.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199911
ED Entered STN: 20000111

Last Updated on STN: 20000111
Entered Medline: 19991124

AB BACKGROUND: Cholinergic agents produce analgesia after systemic and intrathecal administration. A retrospective review showed that intrathecal neostigmine was more potent in women than in men, suggesting a sex difference in this response. The purpose of this study was to determine whether such a sex difference exists in normal rats and to examine the pharmacologic mechanisms that underlie this difference. METHODS: Male and female rats with indwelling intrathecal catheters received injections of neostigmine, bethanechol (muscarinic agonist), or **RJR-2403** (neuronal nicotinic agonist) alone or with atropine (muscarinic antagonist), mecamylamine (nicotinic antagonist), or phentolamine alpha-adrenergic antagonist) with antinociception determined to a noxious heat stimulus to the hind paw. Time versus subcutaneous paw temperature relationships were defined for males and females. RESULTS: Neostigmine produced dose-dependent antinociception with five times greater potency in female than in male rats. Neostigmine-induced antinociception was reversed in male rats by atropine and unaffected by mecamylamine, whereas it was partially reduced by each antagonist alone in females and completely reversed after injection of both. **RJR-2403** was more potent in females than in males, whereas there was no sex difference to bethanechol. Phentolamine partially reversed antinociception from **RJR-2403** in females. Paw temperature increased more rapidly in females than in males for the same lamp intensity. CONCLUSIONS: These data demonstrate a large sex difference in antinociception to intrathecal neostigmine that is primarily the result of a nicotinic component in females. Phentolamine reversal suggests that part of this nicotinic component may rely on spinal norepinephrine release. A better understanding of this sex difference could lead to development of novel pain therapy for women.

CT Check Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Analgesics: AD, administration & dosage
*Analgesics: PD, pharmacology
Cholinergic Agents: AD, administration & dosage
*Cholinergic Agents: PD, pharmacology
Dose-Response Relationship, Drug
Injections, Spinal
Muscarinic Agonists: AD, administration & dosage
Muscarinic Agonists: PD, pharmacology
Muscarinic Antagonists: AD, administration & dosage
Muscarinic Antagonists: PD, pharmacology
Neostigmine: AD, administration & dosage
*Neostigmine: PD, pharmacology
Nicotinic Agonists: AD, administration & dosage
Nicotinic Agonists: PD, pharmacology
Nicotinic Antagonists: AD, administration & dosage
Nicotinic Antagonists: PD, pharmacology
Pain Measurement
Rats
Rats, Sprague-Dawley
***Receptors, Nicotinic: DE, drug effects**
Reference Values
Sex Factors

RN 59-99-4 (Neostigmine)

CN 0 (Analgesics); 0 (Cholinergic Agents); 0 (Muscarinic Agonists); 0 (Muscarinic Antagonists); 0 (Nicotinic Agonists); 0 (Nicotinic Antagonists); 0 (Receptors, Nicotinic)

L176 ANSWER 14 OF 22 MEDLINE
AN 1999421927 MEDLINE
DN 99421927 PubMed ID: 10490929
TI Antinociceptive and pharmacological effects of **metanicotine**, a

selective nicotinic agonist.
AU Damaj M I; Glassco W; Aceto M 'D; Martin B R
CS Department of Pharmacology and Toxicology, Medical College of Virginia of Virginia Commonwealth University, Richmond, Virginia, USA..
mdamaj@hsc.vcu.edu
NC DA-05274 (NIDA)
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1999 Oct) 291 (1) 390-8.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991012
AB **Metanicotine** [N-methyl-4-(3-pyridinyl)-3-butene-1-amine], a novel neuronal nicotinic agonist, was found to bind with high affinity (K(i) = 24 nM) to rat brain [(3)H]nicotine binding sites and it generalized to nicotine in a dose-dependent manner in the drug discrimination procedure. **Metanicotine** produced significant antinociceptive effects in mice and rats subjected to either acute thermal (tail-flick), mechanical (paw-pressure), chemical (para-phenylquinone), persistent (Formalin), and chronic (arthritis) pain stimuli. **Metanicotine** was about 5-fold less potent than nicotine in the tail-flick test after s.c administration, but slightly more potent after central administration. Its duration of action was longer than that of nicotine. Nicotinic antagonists, mecamylamine and dihydro-beta-erythroidine, blocked **metanicotine**-induced antinociception in the different pain models. However, the antinociceptive effect was not affected by pretreatment with either naloxone or by atropine, confirming that **metanicotine** exerts its antinociceptive effect via nicotinic rather than either opioid or muscarinic mechanisms. In contrast to nicotine, antinociceptive effects of **metanicotine** were observed at doses that had virtually no effect on spontaneous activity and body temperature in mice. These data indicate that **metanicotine** is a centrally acting neuronal nicotinic agonist with preferential antinociceptive effects in animals. Thus, **metanicotine** and related nicotinic agonists may have great potential for development as a new class of analgesics.
CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.
*Analgesics: PD, pharmacology
Binding, Competitive
Body Temperature: DE, drug effects
Discrimination Learning
Mice
Mice, Inbred ICR
Motor Activity: DE, drug effects
***Nicotine: AA, analogs & derivatives**
Nicotine: PD, pharmacology
***Nicotinic Agonists: PD, pharmacology**
Pain Measurement
Rats
Rats, Sprague-Dawley
Receptors, Cholinergic: ME, metabolism
RN **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)
CN 0 (Analgesics); 0 (Nicotinic Agonists); 0 (Receptors, Cholinergic)

L176 ANSWER 15 OF 22 MEDLINE
AN 97123118 MEDLINE
DN 97123118 PubMed ID: 8968367
TI **RJR-2403**: a nicotinic agonist with CNS selectivity II.

In vivo characterization.
AU Lippiello P M; Bencherif M; Gray J A; Peters S; Grigoryan G; Hodges H; Collins A C
CS Research & Development Department, R.J. Reynolds Tobacco Company, Winston-Salem, North Carolina, USA.
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1996 Dec) 279 (3) 1422-9.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199701
ED Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970123
AB We have evaluated the physiological and behavioral effects of the CNS-selective nicotinic agonist (E)-N-methyl-4-(3-pyridinyl) -3-butene-1-amine (**RJR-2403**) using a number of different methods, including 1) reversal of pharmacologically induced amnesia in a step-through passive avoidance paradigm, 2) radial arm maze performance in rats with chemically induced brain lesions, 3) changes in HR and blood pressure in rats and 4) changes in body temperature, Y-maze activity, acoustic startle response and respiration in mice. Our results indicate that **RJR-2403** is equal to or better than nicotine on measures of CNS function and cognitive enhancement. Specifically, **RJR-2403** significantly improved passive avoidance retention after scopolamine-induced amnesia and enhanced both working and reference memory in rats with ibotenic acid lesions of the forebrain cholinergic projection system in an 8-arm radial maze paradigm. By comparison, **RJR-2403** was 15 to 30-fold less potent than nicotine in decreasing body temperature, respiration, Y-maze rears and crosses and acoustic startle response. **RJR-2403** also demonstrated greatly reduced cardiovascular effects. **RJR-2403** was approximately 10-fold less potent than nicotine in increasing HR and 20-fold less potent in increasing blood pressure. These results are consistent with in vitro data indicating this compound's high selectivity for CNS nicotinic ACh receptor subtypes relative to peripheral ganglionic and muscle-type nicotinic ACh receptors. Therefore, **RJR-2403** may be a valuable tool for understanding the central and peripheral pharmacology of nicotinic cholinergic systems as well as a potential lead compound for the development of nicotinic therapeutics to treat neurological diseases where cholinergic neurotransmission has been compromised.
CT Check Tags: Animal; Male
Avoidance Learning: DE, drug effects
Blood Pressure: DE, drug effects
***Central Nervous System: DE, drug effects**
Heart Rate: DE, drug effects
Mice
***Nicotine: AA, analogs & derivatives**
Nicotine: ME, metabolism
Nicotine: PD, pharmacology
Nicotinic Agonists: ME, metabolism
***Nicotinic Agonists: PD, pharmacology**
Rats
Rats, Sprague-Dawley
Rats, Wistar
RN **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)
CN 0 (Nicotinic Agonists)

L176 ANSWER 16 OF 22 MEDLINE
AN 97123117 MEDLINE

DN 97123117 PubMed ID: 8968366
TI **RJR-2403**: a nicotinic agonist with CNS selectivity I.
In vitro characterization.
AU Bencherif M; Lovette M E; Fowler K W; Arrington S; Reeves L; Caldwell W S; Lippiello P M
CS Pharmacology Division, R.J. Reynolds Research & Development, Winston-Salem, North Carolina, USA.
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1996 Dec) 279 (3) 1413-21.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199701
ED Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970123
AB Increasing evidence for an involvement of nicotinic cholinergic systems in neurodegenerative disorders has stimulated the search for compounds with selectivity for CNS nicotinic ACh receptors (nAChRs). To this end, we have evaluated a number of nicotinic agonists for their ability to 1) bind to and up-regulate high-affinity nAChRs, 2) release [3H]-dopamine or induce 86Rb+ efflux in synaptosomes, 3) activate nAChRs in PC12 cells, 4) activate muscle-type nAChRs in human TE671/RD cells and 5) induce contraction of guinea pig ileum. Our results indicate that (E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine (**RJR-2403**) binds with high affinity to rat brain cortex (Ki = 26 +/- 3 nM). Functional studies show that **RJR-2403** is comparable to nicotine in activating rat thalamic synaptosomes (EC50 = 732 +/- 155 nM and Emax = 91 +/- 8% for **RJR-2403**; EC50 = 591 +/- 120 nM and Emax = 100 +/- 25% for nicotine) but is one-tenth as potent in inducing dopamine release (EC50 = 938 +/- 172 nM and Emax = 82 +/- 5% for **RJR-2403**; EC50 = 100 +/- 25 nM and Emax = 100 +/- 13% for nicotine). At concentrations up to 1 mM, **RJR-2403** does not significantly activate nAChRs in PC12 cells, muscle type nAChRs or muscarinic receptors. Dose-response curves for agonist-induced ileum contraction indicate that **RJR-2403** is less than one-tenth as potent as nicotine with greatly reduced efficacy. **RJR-2403** does not antagonize nicotine-stimulated muscle or ganglionic nAChR function (IC50 > 1 mM). Chronic exposure of M10 cells to **RJR-2403** (10 microM) results in an up-regulation of high-affinity nAChRs phenomenologically similar to that seen with nicotine. These results suggest that **RJR-2403** interacts with higher potency at CNS nAChR sub-types than at muscle, ganglionic or enteric nAChRs and has higher selectivity for CNS vs. muscle or ganglionic nAChRs than does nicotine.
CT Check Tags: Animal; Female; Human
***Brain: DE, drug effects**
Cell Line
Mice
***Nicotine: AA, analogs & derivatives**
Nicotine: ME, metabolism
Nicotine: PD, pharmacology
Nicotinic Agonists: ME, metabolism
***Nicotinic Agonists: PD, pharmacology**
Rats
Rats, Sprague-Dawley
RN **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)
CN 0 (Nicotinic Agonists)

L176 ANSWER 17 OF 22 MEDLINE
AN 97082235 MEDLINE

DN 97082235 PubMed ID: 8923478
TI A microdialysis study of the effects of the nicotinic agonist **RJR -2403** on cortical release of acetylcholine and biogenic amines.
AU Summers K L; Lippiello P; Giacobini E
CS Department of Pharmacology, Southern Illinois University School of Medicine, Springfield 62794-1222, USA.
NC P30 AG08014 (NIA)
SO NEUROCHEMICAL RESEARCH, (1996 Oct) 21 (10) 1181-6.
Journal code: 7613461. ISSN: 0364-3190.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970514
AB Transcortical dialysis was employed to investigate the effects of subcutaneous (s.c.) injections of **RJR-2403** (1.2-7.2 mumol/kg) on extracellular levels of acetylcholine (ACh), norepinephrine (NE), dopamine (DA), and serotonin (5-HT) in rat. Systemic administration of **RJR-2403** produced a 90% increase of cortical extracellular ACh levels that persisted for up to 90 minutes after injection. Norepinephrine and DA release were increased 124% and 131% above basal values, respectively. Serotonin (5-HT) levels in the dialysate were also significantly elevated by **RJR-2403** (3.6 mumol/kg, s.c.) 70% above baseline at 90 minutes post-injection. Comparison of these responses to those of (-)nicotine from a previous study reveals little difference between the two compounds in their ability to influence cortical neurotransmitter release following systemic administration.
CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Acetylcholine: ME, metabolism
*Biogenic Amines: ME, metabolism
***Cerebral Cortex: DE, drug effects**
Cerebral Cortex: ME, metabolism
Dopamine: ME, metabolism
Dose-Response Relationship, Drug
Microdialysis
***Nicotine: AA, analogs & derivatives**
Nicotine: PD, pharmacology
***Nicotinic Agonists: PD, pharmacology**
Norepinephrine: ME, metabolism
Rats
Rats, Sprague-Dawley
Serotonin: ME, metabolism
RN 50-67-9 (Serotonin); 51-41-2 (Norepinephrine); 51-61-6 (Dopamine); 51-84-3 (Acetylcholine); **538-79-4 (metanicotine)**; 54-11-5 (Nicotine)
CN 0 (Biogenic Amines); 0 (Nicotinic Agonists)

L176 ANSWER 18 OF 22 MEDLINE
AN 96329038 MEDLINE
DN 96329038 PubMed ID: 8739547
TI Relationship between up-regulation of nicotine binding sites in rat brain and delayed cognitive enhancement observed after chronic or acute nicotinic receptor stimulation.
AU Abdulla F A; Bradbury E; Calaminici M R; Lippiello P M; Wonnacott S; Gray J A; Sinden J D
CS Department of Psychology, Institute of Psychiatry, London, UK.
SO PSYCHOPHARMACOLOGY, (1996 Apr) 124 (4) 323-31.
Journal code: 7608025. ISSN: 0033-3158.
CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199611
ED Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961125
AB (-)-Nicotine tartrate (2 mg/kg), and a nicotinic agonist, **RJR 2403** (1.4 mg/kg), and antagonist, mecamylamine (1 mg/kg), were administered to separate groups of rats SC twice daily for 10 days. Two other groups received the same doses of nicotine or **RJR 2403** for 1 day followed by saline for 9 days. Twenty-four hours after the final injection, the rats were compared to a 10-day saline-injected group on acquisition of a hidden platform position in the Morris water maze (20 trials, 30-min inter-trial interval). The rats were killed 48 h after the last drug injection and frontal, entorhinal and posterior cingulate cortex and dorsal and ventral hippocampus assayed for [3H]-nicotine binding density. Chronic nicotine significantly increased the number of frontal and entorhinal cortical and dorsal hippocampal, but not posterior cingulate cortical or ventral hippocampal, nicotinic receptors, and improved rate of learning. Chronic mecamylamine and **RJR 2403** also significantly increased the number of nicotinic receptors in frontal cortex, though not other regions, but retarded rate of learning. Nicotine given for 1 day 11 days earlier marginally increased nicotinic receptors in entorhinal cortex (but not other regions) and significantly increased rate of learning, though significantly less than 10-day nicotine. Entorhinal cortical and dorsal hippocampal nicotinic receptor numbers were positively associated with rate of learning but not performance at asymptote. Thus cognitive enhancement after chronic nicotine is in part a delayed consequence of nicotine administration 11 days earlier, and may reflect regional changes in nicotinic receptor up-regulation.
CT Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
***Brain: DE, drug effects**
Brain: ME, metabolism
***Maze Learning: DE, drug effects**
***Mecamylamine: PD, pharmacology**
Nicotine: ME, metabolism
***Nicotine: PD, pharmacology**
***Nicotinic Agonists: PD, pharmacology**
Rats
Rats, Sprague-Dawley
***Receptors, Nicotinic: DE, drug effects**
Receptors, Nicotinic: ME, metabolism
Up-Regulation
RN 54-11-5 (Nicotine); 60-40-2 (Mecamylamine)
CN 0 (Nicotinic Agonists); 0 (Receptors, Nicotinic)

L176 ANSWER 19 OF 22 MEDLINE
AN 94064839 MEDLINE
DN 94064839 PubMed ID: 8245163
TI Gas chromatographic-mass spectrometric method for determination of anabasine, anatabine and other tobacco alkaloids in urine of smokers and smokeless tobacco users.
AU Jacob P 3rd; Yu L; Liang G; Shulgin A T; Benowitz N L
CS Division of Clinical Pharmacology, University of California, San Francisco 94110.
NC DA01696 (NIDA)
DA02277 (NIDA)
RR-00083 (NCRR)
SO JOURNAL OF CHROMATOGRAPHY, (1993 Sep 8) 619 (1) 49-61.
Journal code: 0427043. ISSN: 0021-9673.
CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199401
ED Entered STN: 19940201
Last Updated on STN: 19980206
Entered Medline: 19940104
AB A selected ion monitoring method for determination of the tobacco alkaloids anabasine, anatabine, nornicotine, **metanicotine**, dihydrometanicotine, and 2,3'-bipyridyl in urine of smokers and smokeless tobacco users is described. The method involves conversion of the secondary amine alkaloids to tertiary amine derivatives by reductive alkylation using an aldehyde and sodium borohydride, and chromatography on a 5% phenylmethylsilicone capillary column. These derivatives have good chromatographic properties, allowing determination of concentrations as low as 1 ng/ml. The alkaloid 2,3'-bipyridyl is unaffected by the derivatization procedure and may be determined simultaneously with the other alkaloids. The structural analogues 2-(3-pyridyl)hexahydroazepine, 5-methyldihydrometanicotine, and 6-methyl-2,3'-bipyridyl were synthesized for use as internal standards. Using the method, concentrations and 24 h excretion of anabasine, anatabine, and nornicotine in urine of twenty-two smokers, eight chewing tobacco users, and six oral snuff users were determined and compared with concentrations and excretion of nicotine and its metabolite cotinine. Excretion of nicotine and cotinine was similar in all tobacco users, but excretion of anabasine, anatabine and nornicotine was substantially greater in urine of smokeless tobacco users, presumably due to absence of pyrolysis of these alkaloids in smokeless tobacco products.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Alkaloids: UR, urine
*Anabasine: UR, urine
Chromatography, High Pressure Liquid
Indicators and Reagents
Mass Fragmentography
*Plants, Toxic
Reference Standards
***Smoking: UR, urine**
*Tobacco, Smokeless
RN 494-52-0 (Anabasine); 581-49-7 (anatabine)
CN 0 (Alkaloids); 0 (Indicators and Reagents)

L176 ANSWER 20 OF 22 MEDLINE
AN 85161837 MEDLINE
DN 85161837 PubMed ID: 3981953
TI Effects of nicotine and its major metabolites on blood pressure in anaesthetized rats.
AU Dominiak P; Fuchs G; von Toth S; Grobecker H
SO KLINISCHE WOCHENSCHRIFT, (1985 Jan 15) 63 (2) 90-2.
Journal code: 2985205R. ISSN: 0023-2173.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198505
ED Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850510
AB Blood pressure and heart rate in anaesthetized rats has been determined after i.v. injection of increasing doses of nicotine (NI) and its major metabolites, i.e. continine (CO), nornicotine (NOR), **metanicotine** (MN) and dihydrometanicotine (DMN). NI and MN elicited similar dose response curves, increasing blood pressure according to the dose injected. However, the dose response curve of MN was shifted to the right.

Furthermore DMN caused similar pressor effects than MN and the pressor effects of NOR was even weaker. Only after injection of CO was a dose-dependent depressor effect observed and this was reversed after very high doses. CO also reduced heart rate in a dose-dependent manner, whereas NI and its other metabolites did not significantly change heart rate.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
*Blood Pressure: DE, drug effects
Cotinine: PD, pharmacology
Dose-Response Relationship, Drug
Nicotine: AA, analogs & derivatives
***Nicotine: PD, pharmacology**
Rats
Rats, Inbred Strains

RN 3000-74-6 (3,4-dihydrometanicotine); 486-56-6 (Cotinine); **538-79-4 (metanicotine)**; 54-11-5 (Nicotine); 5746-86-1 (nornicotine)

L176 ANSWER 21 OF 22 MEDLINE
AN 85010867 MEDLINE
DN 85010867 PubMed ID: 6541274
TI Microcirculatory effects of nicotine and related alkaloids.
AU Henrich H; Hessenauer A; Brune H
SO KLINISCHE WOCHENSCHRIFT, (1984) 62 Suppl 2 92-100.
Journal code: 2985205R. ISSN: 0023-2173.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198411
ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19841109

AB To determine the effects of nicotine alkaloids on the microcirculation of a variety of tissues, we infused equimolar concentrations (10(-4)-10(-1) M) of 1-nicotine (N), nor-nicotine (NN), dihydro-**metanicotine** (DHN) in the skeletal muscle, in a skin flap chamber, and in a saline-perfused mesentery preparation of the rat (WistHan). The qualitative and quantitative responses to these equimolar concentrations were measured by modern microcirculatory techniques. Our data showed that 1-nicotine and its alkaloids differ significantly in dose-dependency, maximal vasoactivity, tissue specificity, and microvascular localization. In conclusion, the small differences in the chemical structure of the pyridine ring which distinguishes the alkaloids cause significantly different microvascular effects.

CT Check Tags: Animal; Comparative Study; Female; Male; Support, Non-U.S. Gov't
Alkaloids: PD, pharmacology
Dose-Response Relationship, Drug
Insecticides: PD, pharmacology
Mesentery: BS, blood supply
*Microcirculation: DE, drug effects
Muscles: BS, blood supply
Nicotine: AA, analogs & derivatives
***Nicotine: PD, pharmacology**
Organ Specificity
Rats
Rats, Inbred Strains
Skin: BS, blood supply
Stereoisomerism
Vasoconstriction

RN 3000-74-6 (3,4-dihydrometanicotine); 532-12-7 (myosmine); 54-11-5 (Nicotine); 5746-86-1 (nornicotine)
CN 0 (Alkaloids); 0 (Insecticides)

L176 ANSWER 22 OF 22 MEDLINE
AN 76171414 MEDLINE
DN 76171414 PubMed ID: 1263119
TI Nicotine-like actions of cis-**metanicotine** and trans-**metanicotine**.
AU Wilson K L Jr; Chang R S; Bowman E R; McKennis H Jr
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1976 Mar) 196 (3) 685-96.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197607
ED Entered STN: 19900313
Last Updated on STN: 19970203
Entered Medline: 19760706
AB The actions of the cis- and trans-isomers of **metanicotine** were observed on isolated rabbit aortic strips and ileal segments. The data are interpreted as showing a nicotine-like action on these preparations for both cis-**metanicotine** and trans-**metanicotine**. This hypothesis is supported in part by the demonstration that the action of the **metanicotine** isomers was affected by hexamethonium, cocaine, phenotolamine, reserpine and atropine in a manner similar to that previously seen in studies with nicotine. In dose-response studies on the aortic strip, trans-**metanicotine** was significantly less active than nicotine. cis-**Metanicotine** in turn was less active than trans-**metanicotine** and nicotine. Additionally, four pyridino compounds, 3-pyridylacet acid, N-(3 pyridlyacetyl) glycine, nicotinuric acid and trans-4-(3-pyridyl)-3-butenoic acid, were tested for both agonist and antagonist activity. No stimulatory activity was found with these compounds in either the aortic strip or ileal preparations. In aortic strip preparations, pretreatment with either 3-pyridylacetic acid or N-(3-pyridylacetyl) glycine provided a moderate to marked reduction in the contractile response to trans-**metanicotine**, whereas pretreatment with trans-4-(3-pyridyl)-3-butenoic acid caused a slight reduction.
CT Check Tags: Animal; In Vitro; Male; Support, U.S. Gov't, P.H.S.
Aorta, Thoracic: DE, drug effects
Atropine: PD, pharmacology
Cocaine: PD, pharmacology
Drug Interactions
Hexamethonium Compounds: PD, pharmacology
Intestines: DE, drug effects
Muscle Contraction: DE, drug effects
***Nicotine: PD, pharmacology**
Phentolamine: PD, pharmacology
Pyridines: PD, pharmacology
Rabbits
Stereoisomerism
RN 50-36-2 (Cocaine); 50-60-2 (Phentolamine); 51-55-8 (Atropine); 54-11-5 (Nicotine)
CN 0 (Hexamethonium Compounds); 0 (Pyridines)

=> d his

(FILE 'HOME' ENTERED AT 08:39:27 ON 04 MAR 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 08:40:07 ON 04 MAR 2003
E METANICOTINE/CN
L1 1 S E3
SEL RN

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L2            4 S E1/CRN

     FILE 'HCAOLD' ENTERED AT 08:40:36 ON 04 MAR 2003
L3           19 S L1 OR L2

     FILE 'HCAPLUS' ENTERED AT 08:41:23 ON 04 MAR 2003
L4           48 S L1 OR L2
L5           77 S METANICOTIN?
L6           17 S PYRIDINE(S)3()4()(METHYLAMINO OR METHYL AMINO)()1()BUTENYL
L7           99 S L4-L6
                E PAPKE R/AU
L8           47 S E3,E4,E6,E7
L9            0 S L7 AND L8
                E NICOTINIC RECEPTOR/CT
                E E6+ALL
L10        7372 S E77,E78,E76+NT
L11        9279 S E81-E87/BI
L12         534 S NICOTINIC (S) RECEPTOR(S) SUBTYP?
L13        6280 S NICOTINIC (S) RECEPTOR(S) (ACETYLCHOLIN? OR ACETYL CHOLIN? OR
L14          18 S L7 AND L10-L13

     FILE 'REGISTRY' ENTERED AT 08:46:31 ON 04 MAR 2003
L15          73 S C10H14N2/MF AND NC5/ES AND 1/NR
L16          13 S L15 AND 3 BUTEN?
L17           5 S L16 AND N METHYL
L18           3 S L17 NOT (D/ELS OR 11C)
L19           2 S L18 NOT L1
                SEL RN
L20           7 S E1-E2/CRN
L21           5 S L20 NOT COMPD
L22           2 S L20 NOT L21

     FILE 'HCAPLUS' ENTERED AT 08:48:13 ON 04 MAR 2003
L23          20 S L19
L24          22 S L21
L25           3 S L22
L26          37 S L23,L24,L25
L27         117 S L7,L26
L28          30 S L10-L13 AND L27
L29       65856 S ACETYLCHOLINE
L30       23900 S NICOTINE
L31          17 S 3 2 4 DIMETHOXYBENZYLIDENE ANABASEINE
L32           4 S DMXB A
L33           7 S 2 METHYL 3 2 (1W) PYRROLIDINYLMETHOXY PYRIDINE
L34           0 S 2 METHYL 3 2 (1W) PYRROLIDINYL METHOXY PYRIDINE
L35          20 S ABT089 OR ABT 089
L36           0 S 3 METHYL S 1 METHYL 2 PYRROLIDINYL ISOXAZOLE
L37          24 S 3 METHYL (1W) 1 METHYL 2 PYRROLIDINYL ISOXAZOLE
L38          80 S ABT418 OR ABT 418
L39           7 S 5 2 AZETIDINYLMETHOXY 2 CHLOROPYRIDINE
L40           0 S 5 2 AZETIDINYL METHOXY 2 CHLOROPYRIDINE
L41          42 S ABT594 OR ABT 594
L42           5 S ALTINICLIN#
L43           0 S 4 2 1 METHYL 2 PYRROLIDINYLETHYL THIO PHENOL HYDROCHLORIDE
L44           0 S 4 2 1 METHYL 2 PYRROLIDINYLETHYL THIOPHENOL HYDROCHLORIDE
L45           0 S 4 2 1 METHYL 2 PYRROLIDINYLETHYLTHIOPHENOL HYDROCHLORIDE
L46           3 S PYRROLIDINYLETHYLTHIOPHENOL OR PYRROLIDINYLETHYLTHIO PHENOL O
L47           9 S SIB1553A OR SIB 1553A
L48           1 S EPIBATADIN#
L49         576 S EPIBATIDIN#
L50        1953 S MECAMYLAMINE

     FILE 'REGISTRY' ENTERED AT 08:58:39 ON 04 MAR 2003
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L51           1 S 51-84-3
L52           1 S 54-11-5
L53          67 S C10H14N2/MF AND NC4/ES AND NC5/ES AND 1/NC AND 2 PYRROLIDINYL
L54          10 S L53 NOT (LABELED OR ION OR 11C# OR 13C# OR 14C# OR C11# OR C1
L55           4 S L54 AND 3
L56          20 S L53 AND NICOTINE
L57           5 S L56 AND L54
                 SEL RN 2 4
L58           3 S L57 NOT E3-E4
L59           4 S L51,L52,L58
L60           1 S L55 NOT L59
L61           5 S L59,L60
L62           1 S 156223-05-1
L63           3 S C19H20N2O2/MF AND 46.150.18/RID AND NC5/ES AND 3/NR AND 2 4 D
L64           1 S 148372-04-7
L65           1 S 148372-04-7/CRN
L66           1 S 161417-03-4
L67          71 S C11H16N2O/MF AND NC4/ES AND NC5/ES
L68           2 S L67 AND 2 PYRROLIDINYLMETHOXY AND 2 METHYL 3
L69           1 S 147402-53-7
L70          10 S C9H14N2O/MF AND NC4/ES AND NOC3/ES
L71           7 S L70 AND 3 METHYL 5
L72           3 S L71 AND 1 METHYL 2
L73           1 S 179120-92-4
L74           4 S C12H14N2/MF AND NC4/ES AND NC5/ES AND 3 ETHYNYL 5
L75           3 S L74 AND 1 METHYL 2
L76           1 S 191611-89-9
L77           1 S 191611-76-4
L78           2 S 140111-52-0 OR 152378-30-8
L79          15 S C11H13CLN2/MF AND 46.156.30/RID AND 103.39.1/RID
L80          10 S L79  AND 6 CHLORO 3
L81           9 S L80 AND 2 6 CHLORO
L82           1 S 826-39-1
L83           1 S 60-40-2
L84           1 S 198283-73-7
L85           9 S C9H11CLN2O/MF AND NC5/ES AND NC3/ES
L86           5 S L85 AND 2 CHLORO
L87           3 S L86 AND 5
L88           2 S L87 NOT 1 METHYL
L89          30 S L61,L62,L64,L65,L66,L68,L69,L72,L73,L75,L76,L77,L78,L81,L82,L
                 SEL RN
L90         402 S E4-E34/CRN
L91         121 S L90 NOT (MXS/CI OR COMPD OR WITH)
L92          84 S L91 NOT (IUM OR CONJUGATE OR COMPLEX)
L93          83 S L92 NOT FE/ELS
L94          79 S L93 NOT CD/ELS
L95          37 S L91 NOT L92
L96          30 S C7H16NO2 AND L95

     FILE 'HCAPLUS' ENTERED AT 10:01:53 ON 04 MAR 2003
L97       43193 S L89 OR L94
L98        2202 S L95,L96
L99          54 S L27 AND L97,L98
L100         16 S L27 AND L31-L50
L101         87 S L27 AND L29,L30
L102         96 S L28,L99-L101
                 E NERVOUS SYSTEM/CT
L103      18878 S NERVOUS SYSTEM/CT (L) (DISORDER OR DISEASE OR DYSFUNCTION)
L104      80095 S ?ALZHEIMER? OR ?PARKINSON? OR ?HUNGTINGTON? OR ?CHOREA? OR ?D
L105      33352 S ?ANXIET? OR ?ANXIOLYT? OR ADDICT? OR (SUBSTANCE OR DRUG OR AL
L106         16 S L27 AND L103-L105
                 E MENTAL/CT
                 E E4+ALL
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L107      27751 S E2+NT
L108     144833 S E10+NT OR E11+NT OR E12+NT
                E E12+ALL
L109       2484 S E5
                E E51
L110      26798 S E23-E77
L111       5763 S E3-E22
L112         11 S L27 AND L107-L111
L113         20 S L106,L112
L114         17 S L102 AND L113
L115         24 S RJR2403 OR RJR 2403
L116         18 S L115 AND L27
L117        123 S L27,L115,L116
L118        101 S L117 AND L10-L13,L29-L50,L97,L98
L119         18 S L118 AND L103-L105,L108-L111
L120          2 S L119 NOT L114
L121        105 S L118-L120,L102,L112-L116
L122         32 S L121 AND (COMPOSITION OR COMBIN? OR MIX? OR SYNERG? OR FORMUL
L123         26 S L122 AND L4,L26
L124         16 S L123 AND L97,L98
L125         10 S L123 NOT L124
L126         73 S L121 NOT L122
L127         18 S L118-L121 AND P/DT
L128         24 S L27 AND P/DT
L129         24 S L127,L128 AND L4-L14,L23-L50,L97-L128
                SEL DN AN 21-24
L130         20 S L129 NOT E1-E12

     FILE 'EMBASE' ENTERED AT 10:47:44 ON 04 MAR 2003
L131         50 S L117
L132         24 S L131 AND (F1. OR F2. OR F3. OR F4.)/CT
                E NERVOUS SYSTEM/CT
L133         35 S L131 AND (E3+NT OR E7+NT OR E11+NT OR E12+NT)
L134          1 S L131 AND (E13+NT OR E22+NT OR E35+NT)
L135          2 S L131 AND E75+NT
                E NERVE/CT
L136          2 S L131 AND E3+NT
L137          6 S L131 AND E50+NT
L138          0 S L131 AND E55+NT
L139          1 S L131 AND E87+NT
L140          0 S L131 AND (E101+NT OR E105+NT)
L141          0 S L131 AND (E108+NT OR E114+NT OR E120+NT)
L142          0 S L131 AND (E132 OR E137+NT)
L143          2 S L131 AND (E146+NT OR E150+NT OR E154+NT)
L144          0 S L131 AND (E164+NT OR E169+NT OR E178)
L145          0 S L131 AND E186+NT
L146          0 S L131 AND E235+NT
L147          0 S L131 AND E263+NT
L148          1 S L131 AND E287+NT
L149          0 S L131 AND E302+NT
L150          0 S L131 AND E335+NT
L151          0 S L131 AND E382+NT
                E ALZHEIMER/CT
                E E10+ALL
L152         14 S L131 AND E1+NT
L153         19 S L131 AND (C2.610. OR C3.220)/CT
                E PARKINSON/CT
                E E5+ALL
L154          4 S L131 AND E1+NT
L155         50 S L131-L154
L156         46 S L29-L50,L89,L94,L95,L96 AND L155
                E NICOTINIC ACETYLCHOLINE RECEPTOR/CT
                E E3+ALL
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                E E2+ALL
L157        6649 S E19+NT
L158          27 S L155 AND L157
L159          27 S L158 AND L156
L160           4 S L155 AND CB/CT
L161           4 S L160 AND L156,L158,L159
L162          46 S L155,L156,L158,L159 NOT L161
L163           9 S L162 NOT AB/FA
L164          37 S L162 NOT L163

     FILE 'HCAPLUS' ENTERED AT 10:59:21 ON 04 MAR 2003

     FILE 'EMBASE' ENTERED AT 10:59:43 ON 04 MAR 2003

     FILE 'REGISTRY' ENTERED AT 11:00:07 ON 04 MAR 2003
L165          14 S L1,L2,L19,L21,L22

     FILE 'MEDLINE' ENTERED AT 11:01:35 ON 04 MAR 2003
L166          10 S L165
L167          22 S L5,L6,L115
L168          22 S L166,L167
L169           7 S L168 AND (F1. OR F2. OR F3. OR F4.)/CT
                E NERVE/CT
                E NERVOUS SYSTEM/CT
                E E3+ALL
L170           9 S L168 AND E3+NT
                E NERVOUS SYSTEM DISEASE/CT
                E E5
L171           2 S L168 AND C10./CT
                E NICOTINIC ACETYLCHOLINE RECEPTOR/CT
                E E3+ALL
L172          11 S L168 AND E2+NT
L173          17 S L169-L172
                E NICOTINIC ANTAGONIST/CT
L174           9 S E4+NT AND L168
                E NICOTINIC /CT
L175          20 S E39+NT AND L168
L176          22 S L168-L175

     FILE 'MEDLINE' ENTERED AT 11:08:14 ON 04 MAR 2003

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FILE 'BIOSIS' ENTERED AT 11:10:19 ON 04 MAR 2003
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RECORDS LAST ADDED: 26 February 2003 (20030226/ED)


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L182 ANSWER 1 OF 4  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN   2002:309819  BIOSIS
DN   PREV200200309819
TI   Enhanced inhibition of a mutant neuronal nicotinic acetylcholine receptor
     by agonists: Protection of function by (E)-N-Methyl-4-(3-pyridinyl)-3-
     butene-1-amine (TC-2403.
AU   Papke, Roger L. (1)
CS   (1) Department of Pharmacology and Therapeutics, University of Florida,
     Gainesville, FL, 32610-0267: rpapke@college.med.ufl.edu USA
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SO Journal of Pharmacology and Experimental Therapeutics, (May, 2002) Vol. 301, No. 2, pp. 765-773. http://jpet.aspetjournals.org. print. ISSN: 0022-3565.
DT Article
LA English
AB Inhibition of neuronal nicotinic receptors can be regulated by sequence in the beta subunit second transmembrane domain (TM2). The incorporation of a beta4(6'F10'T) subunit, which contains sequence from the muscle beta subunit at the TM2 6' and 10' positions of the neuronal beta4 subunit, increases the loss of receptor responsiveness after the application of acetylcholine (ACh), nicotine, or 3-(2,4-dimethoxybenzylidene)-anabaseine (DMXB), an alpha7-selective partial agonist. Inhibition of receptor responsiveness following agonist exposure may occur through either an enhancement of desensitization, increased channel block by an agonist, or alternatively via allosteric modulation. Although DMXB produces very little activation of either alpha3beta4 or alpha3beta4(6'F10'T) receptors, DMXB shows an enhanced use-and voltage-dependent inhibition of alpha3beta4(6'F10'T) receptors compared with wild-type. In contrast, the alpha4beta2-selective agonist (E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine (TC-2403, previously identified as **RJR-2403**) shows increased activation of alpha3beta4(6'F10'T) receptors compared with alpha3beta4 receptors (as related to ACh activation) but with no significant increase in antagonist activity. The interaction between the binding of local anesthetics and the functional inhibition produced by these agonists was evaluated. The binding of the local anesthetics to their inhibitory sites does not affect inhibitory effects of DMXB and nicotine. However, TC-2403 can protect receptor function from the inhibitory effects of other agonists, suggesting that TC-2403, as well as agonists that cause inhibition, may be binding to an allosteric site, either promoting or inhibiting channel opening. The ability of TC-2403 to protect receptor function from agonist-induced inhibition may point toward valuable new combination drug therapies.
CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Reproductive System - Physiology and Biochemistry *16504
Nervous System - Physiology and Biochemistry *20504
Pharmacology - General *22002
Pharmacology - Neuropharmacology *22024
BC Salientia 85306
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
oocytes: reproductive system
IT Chemicals & Biochemicals
3-(2,4-dimethoxybenzylidine)-anabaseine: alpha-7-selective partial agonist; TC-2403 [(E)-N-methyl-4-(3-pyridinyl)-3-butene-1-amine]: alpha-4-beta-2-selective agonist, autonomic - drug, receptor function-protecting effects; acetylcholine; alpha-3-beta-4 receptors; alpha-3-beta-4(6'F10'T) receptors; neuronal nicotinic acetylcholine receptor: enhanced inhibition, mutant; nicotine
IT Methods & Equipment
electrophysiology: analytical method
ORGN Super Taxa
Salientia: Amphibia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Xenopus laevis (Salientia): female
ORGN Organism Superterms
Amphibians; Animals; Chordates; Nonhuman Vertebrates; Vertebrates
RN 51-84-3 (ACETYLCHOLINE)
54-11-5 (NICOTINE)

L182 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:329772 BIOSIS
DN PREV200000329772
TI The activation and inhibition of human nicotinic acetylcholine receptor by **RJR-2403** indicate a selectivity for the alpha4beta2 receptor subtype.
AU **Papke, Roger L. (1)**; Webster, J. Christopher; Lippiello, Patrick M.; Bencherif, Merouane; Francis, Michael M.
CS (1) Department of Pharmacology and Therapeutics, JHMHSC, University of Florida College of Medicine, Gainesville, FL, 32610-0267 USA
SO Journal of Neurochemistry, (July, 2000) Vol. 75, No. 1, pp. 204-216. print.
ISSN: 0022-3042.
DT Article
LA English
SL English
AB Human nicotinic acetylcholine (ACh) receptor subtypes expressed in Xenopus oocytes were characterized in terms of their activation by the experimental agonist **RJR-2403**. Responses to **RJR-2403** were compared with those evoked by ACh and nicotine. These agonists were also characterized in terms of whether application of the drugs had the effect of producing a residual inhibition that was manifest as a decrease in subsequent control responses to ACh measured 5 min after the washout of the drug. For the activation of alpha4beta2 receptors, **RJR-2403** had an efficacy equivalent to that of ACh and was more potent than ACh. **RJR-2403** was less efficacious than ACh for other human receptor subtypes, suggesting that it is a partial agonist for all these receptors. Nicotine activated peak currents in human alpha4beta2 and alpha3beta2 receptors that were 85 and 50% of the respective ACh maximum responses. Nicotine was an efficacious activator of human alpha7 receptors, with a potency similar to ACh, whereas **RJR-2403** had very low potency and efficacy for these receptors. At concentrations of <1 mM, **RJR-2403** did not produce any residual inhibition of subsequent ACh responses for any receptor subtype. In contrast, nicotine produced profound residual inhibition of human alpha4beta2, alpha3beta2, and alpha7 receptors with IC50 values of 150, 200, and 150 muM, respectively. Co-expression of the human alpha5 subunit with alpha3 and beta2 subunits had the effect of producing protracted responses to ACh and increasing residual inhibition by ACh and nicotine but not **RJR-2403**. In conclusion, our results, presented in the context of the complex pharmacology of nicotine for both activating and inhibiting neuronal nicotinic receptor sub-types, suggest that **RJR-2403** will be a potent and relatively selective activator of human alpha4beta2 receptors.
CC Nervous System - General; Methods *20501
Biochemical Studies - General *10060
BC Salientia 85306
Hominidae 86215
IT Major Concepts
Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
RJR-2403: acetylcholine receptor agonist, efficacy; acetylcholine; alpha-3-beta-2 receptors; alpha-4-beta-2 receptor: activation; alpha-7 receptors; nicotine; nicotinic acetylcholine receptor: activation, inhibition
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Salientia: Amphibia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Xenopus (Salientia); human (Hominidae)
ORGN Organism Superterms
Amphibians; Animals; Chordates; Humans; Mammals; Nonhuman Vertebrates;

Primates; Vertebrates
RN **183288-99-5 (RJR-2403)**
51-84-3 (ACETYLCHOLINE)
54-11-5 (NICOTINE)

L182 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:33262 BIOSIS
DN PREV199900033262
TI **RJR-2403** is an efficacious agonist for human alpha4beta2 neuronal nicotinic acetylcholine receptors with lower efficacy for other human receptor subtypes.
AU **Papke, R. L. (1)**; Webster, J. C. (1); Lippiello, P. M.; Bencherif, M.; Francis, M. M.
CS (1) Dep. Pharmacology, Univ. Fla., Coll. Med., J.H.M.H.S.C., Gainesville, FL 32610 USA
SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 88. Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 1 Los Angeles, California, USA November 7-12, 1998 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
CC Pharmacology - General *22002
Biochemical Studies - General *10060
Metabolism - General Metabolism; Metabolic Pathways *13002
Nervous System - General; Methods *20501
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
IT Major Concepts
Nervous System (Neural Coordination); Pharmacology
IT Chemicals & Biochemicals
nicotine; nicotinic acetylcholine receptor: alpha 4 beta 2, human, neuronal; **RJR-2403**
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
RN **183288-99-5 (RJR-2403)**
51-84-3 (ACETYLCHOLINE)
54-11-5 (NICOTINE)

L182 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1996:551881 BIOSIS
DN PREV199699274237
TI In vitro activation of alpha-4 beta-2 nAChR by **RJR-2403** suggests differential desensitization relative to nicotine.
AU Watterson, J. (1); Moulton, B. (1); Lippiello, P.; Bencherif, M.; **Papke, R. L. (1)**
CS (1) Dep. Pharmacol. Therapeutics, Univ. Florida, Gainesville, FL 32610 USA
SO Society for Neuroscience Abstracts, (1996) Vol. 22, No. 1-3, pp. 1269. Meeting Info.: 26th Annual Meeting of the Society for Neuroscience Washington, D.C., USA November 16-21, 1996 ISSN: 0190-5295.
DT Conference
LA English
CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
Pathology, General and Miscellaneous - Therapy *12512
Endocrine System - Neuroendocrinology *17020
Nervous System - Pathology *20506
Pharmacology - Neuropharmacology *22024
BC Animalia - Unspecified *33000
IT Major Concepts
Biochemistry and Molecular Biophysics; Endocrine System (Chemical

Coordination and Homeostasis); Membranes (Cell Biology); Nervous System (Neural Coordination); Pathology; Pharmacology

IT Chemicals & Biochemicals
RJR-2403; NICOTINE

IT Miscellaneous Descriptors
ALZHEIMER'S DISEASE; BEHAVIORAL AND MENTAL DISORDERS; CHOLINERGIC; MEETING ABSTRACT; MEETING POSTER; NERVOUS SYSTEM DISEASE; NICOTINE; NICOTINIC ACETYLCHOLINE RECEPTOR; PARKINSON'S DISEASE; PHARMACOLOGY; **RJR-2403**; THERAPEUTIC DEVELOPMENT

ORGN Super Taxa
Animalia - Unspecified: Animalia

ORGN Organism Name
animal (Animalia - Unspecified); Animalia (Animalia - Unspecified)

ORGN Organism Superterms
animals

RN **183288-99-5 (RJR-2403)**
54-11-5 (NICOTINE)